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NOCTURNAL PSYCHOPATHOLOGY: SLEEP, DREAMING, MOOD AND LIGHT-THERAPY IN BIPOLAR DISORDER

by

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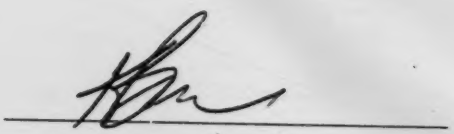

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THE DREAM

Sleep, do not forgo me,
for it is with great anticipation
that I await your adventures.

To you, I entrust my soul each night,
that I should be led
as fate desires,
through dark, ominous corridors
that pull, weight, and try to prevent me;
through fires, floods, and to foe that torment me.

But, your challenges, I, nevertheless welcome,
for they inevitably lead me to escape.
And only here am I momentarily transformed,
empowered and enveloped,
in ecstacy and magic,
of the living and the dead.
Then safely freed and quietly returned,
to the comforts of my bed.

Kathleen M. Beauchemin

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ABSTRACT

In a series of studies, the relationship between circadian rhythm, phototherapy, REM sleep, dreaming, and abnormal mood was demonstrated. In a pilot study, dream content was found to reflect prevailing mood and transitions in mood state in bipolar disorder. To replicate and extend initial findings, sleep, dream content, and mood was then monitored in both bipolar and unipolar patients hospitalized for depression. Sleep was recorded intermittently using the Nightcap, a computerized ambulatory sleep monitoring device, which afforded a record of patients' sleep during several seemingly abrupt nocturnal mood changes. Two further studies demonstrated that phototherapy is an effective adjuvant treatment strategy for non-seasonal depressive disorders. Both unipolar and bipolar depressions responded to phototherapy and degree of mood improvement corresponded to the intensity of illumination. This was demonstrated in both artificial and natural lighting paradigms. Finally, a subset of participants had their sleep monitored before and after light treatment in order to determine the impact, if any, of phototherapy on sleep. Although subjects reported feeling less tired following phototherapy, no measurable changes in sleep were detected. The composite results of these five studies suggest that:

(i) dream content systematically relates to prevailing mood state, but patterns are different in unipolars and bipolars;

(ii) dreams of death are frequent in bipolar disorder and mark the transition of a mood shift upward.

(iii) REM latency is reduced in both depressed unipolars and bipolars but tends to increase as mood improves in bipolars.

(iv) Phototherapy (both natural and artificial) is an effective adjuvant for the treatment of depression, and commonly used light intensities are suboptimal.

(v) The mechanism of action by which light exerts its beneficial effects remains unclear but appears to not be related to objective alterations in sleep.

This thesis encompasses a wide-ranging scope: circadian rhythm, phototherapy, sleep, REM sleep, dream content, and mood. A review of the general area is offered and the results of several research studies are reported. Finally, a conclusion and tentative hypothesis about the nature of the relationship between these variables is offered.

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I would especially like to express my appreciation to my primary supervisor Dr. Peter Hays who gave me hours of invaluable advice and guidance but at the same time the freedom to explore my own ideas. I am also very grateful to all those patients who candidly shared their lives with me, leaving me with tremendous admiration, empathy and insight into the ongoing struggles one faces in the control of a mood disorder.

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LIST OF SYMBOLS AND ABBREVIATIONS

ACh:	Acetylcholine
ACTH:	Adrenocorticotropic hormone
BD:	Bipolar disorder (previously called manic-depression)
D-SLEEP:	Desynchronized sleep (REM)
DA:	Dopamine
DSM-IV:	Diagnostic & Statistical Manual of Mental Disorders (4th Ed)
ECT:	Electro-convulsive therapy
EEG:	Electroencephalogram
EMG:	Electromyogram
EOG:	Electrooculogram
5-HT:	5-hydroxytryptamine (serotonin)
FTG:	Gigantocellular tegmental field (fastigial tegmental)
LC:	Locus ceruleus
MAO:	Monoamine Oxidase
MDD:	Major depressive disorder
MEL:	Melatonin
MEMA:	Middle Ear muscle activity
mPRF:	Medial pontine reticular formation
NA:	Noradrenaline
NREM:	Non-rapid-eye-movement
PGO:	Ponto-geniculo-occipital waves
PIPs:	Phasic integrated potentials
POMS:	Profile of mood states
PRF:	Pontine reticular formation
REM:	Rapid-eye-movement
RI:	Reciprocal interaction model of REM/NREM sleep
SSRI:	Selective serotonin reuptake inhibitor
SWS:	Slow wave sleep

1.0 CHAPTER 1

GENERAL INTRODUCTION

1.1 FOREWORD

The focal topic of this thesis is an in-depth analysis of the relationship between REM sleep, dreaming, and mood in bipolar disorder. However, these phenomena can not adequately be isolated, nor can they be adequately reviewed or studied as if they are distinct from the environment in which they occur and the corollary factors with which they relate, namely: circadian rhythm, sleep in its entirety, and mood treatment strategies. Yet a thesis which encompasses circadian rhythm, sleep, REM sleep, dreaming and mood therapies (specifically phototherapy), combining a variety of experimental and descriptive approaches has the potential to be more confusing than rewarding. Therefore, I shall proceed in as orderly a fashion as possible, going from the general to the particular, as follows.

A description of normal circadian rhythm, sleep, and dreaming will precede an account of mood disorders and their treatments, followed by circadian rhythm, sleep, and dreaming when mood is disturbed. Subsequently, on the basis of this infrastructure, the logic of the experimental reports will be apparent, and the results, though some were unexpected, coherent. The conclusions should arise naturally from the forgoing, and the discussion will utilize only those concepts and data which have been reported earlier in the thesis.

The first chapter is intended as a comprehensive introduction to the general area in question. However, prior to launching into great detail, a brief overview of the history of dreaming is offered.

1.2 DREAMING FROM PAST TO PRESENT

Enormous amounts of time and ingenuity were invested in the theories of dreaming and the interpretation of dreams over the centuries, but the work and its fruits were poetic rather than systematic or empirical. The analysis of dream content dates back as far as 5000 BC (Miller, 1978). Dreams were once held to be a divine experience in which the soul left the body to communicate with the gods. Artemidorus, a second century philosopher compiled a series of books on dream interpretation called Oneircritica in which dreams were said to be prognostic symbols (White, 1975), a tradition that lingers in pseudo-scientific literature today. For example:

> To dream of [the] dead, warns you of coming dissolution or sorrow. Disappointments always follow dreams of this nature. To hear of any friend or relative being dead, you will soon have bad news from some of them. [These dreams] frequently occur when the dreamer is controlled by imaginary states of evil or good. A man in that state is not himself, but is what the dominating influence make

him (cited in, Miller, 1978; p 187).

One of the first serious considerations of dreaming as a scientific topic was pursued by Aristotle (1933) who tried to dispel the earlier assumption that dreaming occurred by way of super-natural or spiritual influences. He attributed dreaming, instead, to natural causes within sleep. Freud, undoubtedly influenced by Aristotle's writings, and using a similar intuitive and non-experimental approach, wrote with vigour about dreaming in the *Interpretation of Dreams* (1900; 1991 new edition). It was not until the advent of the discovery of REM sleep by Aserinsky and Kleitman (1953) in the nineteen-fifties that dreaming and its accompanying neurophysiology became the subject of serious scientific pursuit. With the aid of modern technology, many old ideas about sleep and dreaming have been refuted.

The artistic method is different from the scientific, but its hypotheses are not necessarily wrong. For example, Freud's (1991) claim that "a first outbreak of delusional insanity often originates in a terrifying dream" (p. 160) is supported in contemporary findings, including our own (Beauchemin & Hays, 1995). In Hartmann's (1984) work with nightmare sufferers, he noted that subjects reported frequent nightmares prior to a psychotic episode.

Hippocrates' (1923) claim that dream content can serve as a diagnostic guide by externalizing an internal process is another ancient assertion with some modern support. For example, patients with ulcers and hypertension report elevated tendencies in aggression and hostility in their dream content

(Smith, 1984). In a retrospective study, dreams of death and destruction heralded a poor prognosis in cardiovascular patients (Smith, 1991). In his warning theory of dreams, Smith (1991) concludes that the severity of the illness is reflected in dream content:

> Dreams with references to death [in males] and separation [in females] are associated with more severe underlying dysfunction of the dreamer (p.138).

Historically, dream research held a prominent place in psychoanalytic theory. Today the study of dreaming falls into two main categories: dream physiology and dream psychology. Dream physiology concerns itself with the physiological concomitant of dreaming, whereas dream psychology tends to focus on the cognitive experience and content of the dream (Smith, 1991). Whereas psychoanalytic interest focused mainly on the so called "latent" or disguised meaning of dreams, recent focus has shifted towards a greater consideration of the "manifest" or more obvious meaning of dreams (Cartwright & Lambert, 1992).

As neurophysiological correlates of brain activity in sleep became identified over the last few decades, dreaming, as a research topic, gained credibility in neurophysiology and neuropsychology. Since the discovery of REM sleep, a drastic change has transpired in the once held view of sleep as a passive state. REM dreaming is now recognized as a very active brain state. Although active thought processes occur throughout sleep, REM

dreaming appears to represent a particularly intense state, both psychologically and physiologically.

Despite substantial progress in the identification of biological correlates to mental states, these two paradigms of dream research (neurophysiological and psychological) are often pursued divergently. Psychological and physiological theories of dreaming need not be divergent. Unless one maintains the antiquated view of mind-body dualism, mental states are, necessarily, rooted in physiology.

In an attempt to bridge psychoanalysis with neurophysiology, Lehtonen (1980) writes:

> Phylogenetically archaic parts of the brain, like the brain stem, mesencephalon, diencephalon, and the limbic system play an important part in regulating paradoxical sleep.... A qualitative regression takes place in the direction of a less organized state. The biological memory function is also activated during paradoxical sleep. The aim of this perhaps is reorganization and consolidation of memory traces through nocturnal processing of the material derived from the experiences of the previous day. Neuronal memory processing, which has also been investigated at the chemical, monoaminergic level, probably has

significance [in] the development of memory and other psychic functions (p. 419)

Despite decades of scientific research on sleep and dreaming since Freud's first account, including the discovery of REM sleep, we have yet to determine the precise function or purpose of sleep or dreaming (assuming that one actually exists). Many theories have been proposed and these will be discussed fully in the chapters to follow. One particular hypothesis about the role of dreaming that will be central to this discourse is that of Milton Kramer, (1993) and of Michael Perlis & colleagues (Perlis & Nielsen, 1993; Perlis, Giles, Flemming, et al., 1995) who propose a mood regulatory function for dreaming. In essence, the work undertaken for this dissertation tests this very assumption: that dreaming serves to regulate mood and that a failure in this function (nocturnal psychopathology) can result in waking psychopathology. This assumption, however, is not based on a linear model of causation, per se, as it is assumed that waking state itself also serve to alter the sleep experience and therefore a reciprocal connection is undoubtedly involved.

The following dissertation is intended as a comprehensive report of research undertaken for the purpose of logical and systematic identification and description of the relationship between circadian rhythm, REM sleep, dreaming, mood, and phototherapy as a mood treatment in psychiatric patients with depressive illnesses. A general discussion and literature

review on pertinent aspects of circadian rhythm, human sleep, dreaming and mood disorders is presented and finally, specific methodological reports of several related studies that were undertaken follows. The first two studies examine the relationship between dreaming and mood in bipolar disorder. The third and forth studies were undertaken, in part, to establish the credibility of phototherapy for the experimental manipulation of mood as it relates to the initial studies; and in doing so, demonstrating alternative treatment strategies for depression.

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CHAPTER 2

A REVIEW OF ENDOGENOUS BIOLOGICAL RHYTHMS, SLEEP, DREAMING, MOOD & MOOD THERAPIES

PART 1: STATE OF THE KNOWLEDGE

2.1 BIOLOGICAL RHYTHMS

Turek and Van Reeth (1995) write that: "one of the most obvious adaptive features of living organisms on earth is the ability to change behavior on a 24 hour basis (p. 1329)." Although the existence of biological rhythms was alluded to as far back as 4th century BC, these observations were restricted to plants and presumed to be a passive response to environmental changes (Halaris, 1987). However, in 1880, Darwin (cited in Halaris, 1987) postulated that changes in plant life remain periodic and were endogenous, i.e., persisted in the absence of environmental cues. In 1906, Simpson and Galbraith (cited in Halaris, 1987) demonstrated that temperature rhythms were endogenous in monkeys and that the light-dark cycle entrained or synchronized biological rhythms. Humans were assumed to be distinct from the influence of environmental factors on circadian rhythm until the 1960s where several studies conducted in temporal isolation proved differently. Since then, specific oscillators or drivers of circadian rhythms have been postulated, identified, and isolated. Virtually all chronobiologists now agree that circadian rhythms are produced and driven by endogenous pacemakers and that these pacemakers rely on environmental

and social cues for synchronization and entrainment (Nir, 1995). While some behavioral diurnal fluctuations are readily apparent, such as the sleep-wake cycle, many more subtle physiological changes underlie rhythmic behavioral changes.

Biological rhythms are generally classified into four broad categories:

(1) ***CIRCANNUAL***: These are changes that occur on an annual basis, such as breeding and hibernation as evidenced in some animal species. Although humans are not subject to circannual rhythms, per se, one might argue that the regularly occurring fluctuation in mood seen in Seasonal Affective Disorder and other mood disorders with a seasonal component might be a variant or vestige of this phenomenon.

(2) ***INFRADIAN:*** Infradian rhythms are those that occur beyond daily, and are often monthly or bimonthly. Activity levels of marine animals, for example, are said to fluctuate according to bimonthly changes in the tides (Wade & Travis, 1996). Regularly occurring hormonal fluctuation of the female menstrual cycle on a 28 day cycle is an example of a human infradian rhythm.

(3) ***CIRCADIAN:*** These rhythms occur approximately every 24 hours. A classic example of this rhythm is that of the sleep-wake cycle. This cycle occurs in consort with the fluctuation of numerous physiological phenomena, such as body temperature, melatonin, and cortisol secretion.

(4) ***ULTRADIAN:*** Ultradian rhythms occur more than once per day. In

humans, ultradian rhythms follow a cycle of approximately 90 minutes. One ultradian rhythm of interest that will be discussed at length is the REM / NREM (rapid-eye-movement & non-rapid-eye-movement) sleep cycle. There is also some evidence that mood and alertness may wax and wane in 90 minute waves.

The primary biological rhythms of central importance to the topic of this discourse are: circadian (as it relates to sleep) and ultradian (as it relates to REM sleep). These will subsequently be discussed in greater detail, starting with circadian rhythm. The discussion of ultradian rhythm will be withheld for the moment and later intertwined with the discussion of REM sleep.

2.2 THE GENERATION AND ENTRAINMENT OF CIRCADIAN RHYTHM

Circadian rhythm arises in a cyclical manner that is approximately but not precisely 24 hours. Hence, the term circadian is derived from Latin *Circa Diem* meaning *about a day*. Fluctuation in sleep-wake, temperature, locomotor activity, and various hormonal and neurochemical substrates are subject to diurnal patterns of expression. There are variations among species but the discussion will be limited to humans unless otherwise specified.

Circadian rhythm is believed to occur by endogenous regulatory mechanisms. Evidence for their endogenous nature comes primarily from

animal and laboratory studies that demonstrate continuity in these rhythms in the absence of external cues. Endogenous control of temperature, melatonin secretion, and cortisol secretion in addition to regular periodic sleep has been demonstrated in human subjects. When subjects are deprived of all external zeitgebers (exogenous time cues), they continue to follow a circadian pattern in sleep, temperature and hormonal fluctuations, suggesting endogenous control, but these cycles begin to show a gradual prolongation towards 25 or more hours. Under such conditions, circadian rhythm is referred to as "free-running".

In a classic experiment by Kleitman (1963), an attempt was made to artificially lengthen subjects' endogenous rhythms. Two male volunteers spent a month living in total isolation in a deep Kentucky cave with an artificially imposed 28 hour sleep wake cycle. One subject gradually adjusted with body temperature fluctuating closely in-sync with his sleep-wake cycle. The other subject's temperature rhythm continued to persist in a 24 hour manner resulting in an uncoupling of temperature rhythm and imposed sleep-wake cycle. He reported great difficulty falling asleep and then waking at imposed times. On the basis of this, and other experiments, it would appear that humans, although fairly consistent, are subject to individual variation in both the length and strength of their endogenous rhythms and in their ability to adapt to environmental changes.

2.3 ENDOGENOUS PACEMAKERS

It has been clearly established that there is periodic rhythmicity of numerous variables such as: sleep-wake, body temperature, hormone secretion, urinary volume, and sensitivity to drugs (Moore-Ede, Czeisler & Richardson, 1983). However, whether these fluctuations are driven by one or more endogenous oscillators has been debated. It would appear that humans have at least two endogenous oscillators or "biological clocks" (Kalat, 1992); however, one, the suprachiasmatic nucleus, is presumed to be a master oscillator; the other(s) (not specified) considered subordinate. As mentioned previously, both animal and human subjects who are isolated from zeitgebers become free-running. When this occurs, hormone secretion, eating, drinking, urination and locomotor activity tend to stay closely aligned with the sleep-wake cycle adopted; however, body temperature does not, suggesting that there may be separate pacemakers driving sleep and temperature cycles.

Two discrete nuclei that are referred to as the suprachiasmatic nuclei (SCN) are located in the anterior ventral hypothalamus, immediately above the optic chiasm. The SCN is thought to regulate most, if not all, circadian rhythms in mammals and to function as the master pacemaker.

> The SCN clearly functions as the executive clock in mammals, and there is no convincing evidence that any other area in the brain can function as a master circadian pacemaker or that a timing system anywhere else in the

brain can be entrained by the light-dark cycle (Turek & Van Reeth, 1995; p. 1334).

Evidence for the executive role of the SCN in circadian rhythm control comes primarily from animal lesion studies. Destruction of the SCN leads to severe disruption or complete abolishment of many internal rhythms, including: body temperature, sleep-wake cycle, cortisol, pineal melatonin, and growth hormone secretion (Stephen & Zucker, 1972; Moore & Eichler, 1972). In addition, fetal SCN tissue transplants can restore arrythmic lesioned rodents (DeCoursey & Buggy, 1988).

One major pathway to the SCN is the retinohypothalamic tract which likely provides information about environmental lighting conditions to the SCN (Nir, 1995). There are numerous afferent inputs from other brain areas including: the hypothalamus, thalamus, septum, midbrain raphe nuclei; efferent destinations include the limbic system and the pineal gland, which via a complex sympathetic chain, regulates melatonin secretion (Mendelson, 1987).

2.4 CIRCADIAN RHYTHM AND SLEEP

In an earlier model of circadian rhythm, it was suggested that sleep occurs when a controlling circadian oscillator falls below a fixed point (Wever, cited in Mendelson, 1987). However, this model failed to account for possible desynchronization of circadian rhythm resulting from sleep-phase

shifting. It also did not account for the ability to voluntarily impose wakefulness despite circadian priming, such as when working shift-work. Finally, this model did not address the occurrence of two distinct types of sleep, namely, REM sleep and NREM sleep, both of which appear to operate under different control mechanisms. Perhaps in light of these shortcomings, this model was expanded to suggest that two pacemakers exist: (X) which is said to regulate temperature, cortisol secretion, and REM sleep, and (Y) a weaker pacemaker that governs the sleep-wake cycle (Wever, 1975). Environmental zeitgebers are presumed to affect the (Y) oscillator.

An alternate model was later proposed by Borbely (Borbely, 1982; Hauri, 1992). This model combines homeostatic and circadian principles. The model is as follows: process S is described as a sleep-regulating variable that accumulates during wakefulness. Although S is not clearly defined, it is presumed to be a hypnotoxin or soporific such as delta-sleep-inducing peptide. Although not explicitly stated as such, melatonin may also fit this role. One measurable manifestation of S is believed to be the propensity or power of delta slow wave sleep (defined later). Then, a second factor, process C, is the circadian system, which may correspond to the SCN, which functions as the master circadian clock.

> Thus in this model, there is a single pacemaker that, under normal conditions, is entrained daily by external time cues. This circadian process imposes a rhythm on a variety of

> physiological activities and could conceivably synchronize other systems that have their own rhythm [such as temperature]. Sleep onset would occur when the gradual rising of process S intercepts a threshold determined by process C (Mendelson, 1987; p.301)

One major variable with a circadian rhythm is endogenous temperature. Sleep onset occurs as temperature falls, and temperature continues to fall until the early morning hours. The duration of sleep and the occurrence of REM sleep appears to be connected to the temperature phase. Most REM sleep occurs at the nadir of the temperature cycle and waking accompanies a temperature rise (Hauri, 1992). The direction of this relationship is, however, unclear. It may be that temperature is a passive player and rises and falls as a consequence of level of alertness (Wang, 1997; personal communication).

In fact, one hypothesized function of sleep is to decrease body temperature (Sasaki, Miyasita, Takeuchi, et al., 1993).

2.5 SLEEP

Sleep might be viewed as the universal prototype of circadian rhythm. Although sleep is clearly modulated by brain centres that drive internal rhythms, to date:

> It has not been possible to completely eliminate NREM sleep

by destruction of a single brainstem region. Control of NREM sleep likely resides in widely ranging circuits from the area around the solitary tract in the medulla through the dorsal raphe nucleus to the basal forebrain area (Hauri, 1992; p8).

For sleep to occur, systems of wakefulness (the reticular activating system) must subside so that the weaker sleep system can dominate (Hauri, 1992).

2.5.1 The function of sleep:

Despite great advances in the field of sleep research, no definitive function of sleep has yet been agreed upon. Most, however, would agree that some function must exist considering the pervasive influence of sleep on our daily lives. Various theories of the putative functions of sleep have been proposed.

2.5.2 Sleep is restorative:

The most commonly subscribed view of the function of sleep is that it is a biological imperative for restoration. This model is based on the assumption that sleep facilitates some regenerative process such as tissue growth and repair (Moorcroft, 1989). There is some evidence in support of this theory. For example:

Animal studies show that mitosis of epithelial cells of

> many body tissue occurs preferentially during sleep. Also there is an increase in protein synthesis at this time. Other studies have shown that the healing of wounds is faster during sleep, as is bone growth (Moorcroft, 1989; p. 308).

Additional support for this model involves the associated hormonal activity linked to sleep. Growth hormone is believed to be released specifically following the first delta sleep period of the night. This relationship is particularly strong in early life, for example in neonates, where delta sleep is more abundant. As delta sleep tapers off in late life, so does the concomitant release of growth hormone. Other anabolic hormones such as prolactin, melatonin, luteinizing hormone, and testosterone also show higher levels in sleep, while in contrast, catabolic hormones, such as corticosteroids are lowest (Moorcroft, 1989). It has also been reported that the greater the metabolic demands of prior wakefulness, the longer the subsequent total sleep time, in particular delta sleep (Moorcroft, 1989). The need for sleep is often lengthened considerably by systemic infection and disease (Krueger, Toth, Johannsen & Opp, 1990).

Finally, we can infer a restorative function from studies involving sleep deprivation. A classical technique for determining the function of a physiological process is to remove or prohibit its occurrence and then observe and record the consequences (Mendelson, 1987). In animal studies, total

sleep deprivation results in death in as little as 33 days (Rechtschaffen, Gilliland, Bergmann, & Winter, 1983). Human accounts vary, and are naturally limited by ethical constraint; but all show at least transient detrimental consequences on mood, cognition, and performance for partial or total sleep loss in normal subjects. More severe consequences, such as paranoia, delusions, hallucinations and other forms of psychoses have also been reported following prolonged wakefulness (Dement, 1978; Luce & Segal, 1966). In addition, a strong "rebound" of compensatory sleep immediately follows its deprivation (Carskadon & Dement, 1994). An acquired sleep disorder known as Fatal Familial Insomnia results in profound neurological pathology and eventual death following prolonged sleep deprivation (Fleming, Feldman, Green, et al., 1996).

2.5.3 Sleep as an evolutionary behaviour:

Another view of sleep is based on phylogeny. It is theorized that sleep is an adaptive evolutionary behaviour designed to protect and accommodate the organism's survival. Thus, according to this theory, the primary function of sleep is to promote the conservation of energy when we would otherwise be relatively inefficient and vulnerable (Kleitman, 1963). It has been suggested that humans sleep for an extended period at night because this behaviour has evolved from what was once a necessary protective measure to ensure safety from nocturnal carnivorous predictors (Kelly, 1985). This theory's

premises would suggest that animal species should vary in how much sleep is needed depending on such factors as time spent in search and gather of food and level of presumed danger from predators during sleep. To some degree, this assumption is supported, in that those species at high risk from predators, such as goats and sheep, do tend to sleep very little (Kalat, 1992). However, despite their vulnerability, the fact that they do sleep (as do all species) is indicative of some underlying survival value of sleep (Hauri, 1979). Humans tend to be drifting towards having shorter sleep time; however, this is likely to be a direct reflection of the corresponding advances of technology and, specifically, the artificial lengthening of daylight afforded by electricity.

As a general rule, human adults sleep about 7 to 8 hours per day. However, this is subject to vast individual differences ranging from about 6 or less to 11 or more hours per day (Moorcrcft, 1989). The general clinical rule is that an adequate amount of sleep is determined solely on the basis of a person's ability to feel reasonably alert throughout the intervening wakeful period. Individual differences are likely to arise from social, behavioral, and genetic influences.

2.5.4 Human sleep architecture and measurement:

The multimodal physiological recording of sleep is referred to as polysomnography. This is comprised of the electroencephalogram (EEG),

which measures surface electrical activity or brain waves (Johnson, 1977), the electro-oculogram (EOG), which detects eye movements, and the electro-myogram (EMG), which detects muscle activity. A basic sleep recording requires three bipolar electrode placements: one pair records a one channel EEG, one pair records eye movements (EOG), and one pair records muscle movements (EMG). An additional pair of electrodes are placed on the ear lobes to serve as referents (Hauri, 1982).

From these measures, recordings can be divided by distinct characteristics into sleep stages. Sleep is broadly divided into NREM and REM sleep. NREM is further divided into 4 progressively deepening stages. Stage 1 NREM sleep consists of low-amplitude, mixed frequency EEG recordings. In stage 2, low-amplitude, mixed-frequency recordings continue, but in addition, K-complexes and intermittent bursts of sleep spindles appear. K-complexes are high amplitude, sharp negative waves followed by a slower positive wave over a duration of approximately half a second. These are seen as sharp upward deflections on the recording. Sleep spindles are bursts of rhythmic activity of 12-14 Hz lasting at least half a second (Moorcroft, 1989).

In stages 3 and 4, the EEG displays progressively more delta waves of an increasing amplitude. These stages are commonly referred to as slow wave sleep (SWS). Stages 1 to 4 are collectively referred to as NREM sleep. Other nomenclature used to describe NREM sleep are quiet-sleep, s-sleep,

orthodox sleep, and delta-sleep. Technically, SWS is restricted in reference to stages 3 and 4 (Moorcroft, 1989).

Following an initial progression from stages 1 to 4, the recording returns to stage 2 and from there, the sleeper typically enters the first REM episode of the night. Following a short burst of REM sleep, the sleeper then alternates between REM and NREM sleep for the remainder of the night (Johnson, 1977; Kelly, 1985). REM sleep continues to occur in cyclical epochs, approximately every 90 minutes, cumulatively occupying 20-25% of total sleep time in a normal adult (Kelly, 1985). The EEG pattern during REM resembles that of stage 1, except for the presence of sawtooth waves, and the appearance of rapid conjugate eye movements in the EOG. REM sleep is sometimes referred to as paradoxical sleep, in that brain activity closely resembles that of being awake, yet arousal threshold is high, suggesting that in some respects REM sleep is a "deep" stage of sleep.

2.6 REM SLEEP & DREAMING

2.6.1 What is REM sleep?

REM sleep is a distinct psychophysiological phenomenon that occurs cyclically in discrete episodes of increasing length and intensity during sleep (Carskadon & Dement, 1994). Its cyclic rhythm is ultradian in nature, occurring approximately every 90 minutes throughout sleep. REM sleep is characterized by: (1) intense neuronal activation, (2) low voltage

desynchronized EEG recordings, (3) rapid conjugate eye movements, (4) profound muscle atonia, (5) increased or irregular heart rate, blood pressure, and breathing, (6) penile tumescence in males (Jones, 1970) and increased vaginal secretion in females (Kalat, 1992). Awakenings from REM sleep habitually elicit reports of dreaming (Kelly, 1985).

REM sleep is sometimes alternately referred to as paradoxical sleep, active sleep, desynchronized or d-sleep, and dream sleep (Siegel, 1994). Inherent in each of these terms is an underlying assumption, perhaps bias, of what the defining features of this state are assumed to be. But for the most part, it is a question of semantics.

In human adults, REM sleep is identified by the simultaneous presence of a desynchronized (i.e., relatively low voltage with mixed frequency) cortical EEG, an absence of large muscle movements (atonia), and periodic bursts of rapid conjugate eye movements (Siegel, 1994).

2.6.2 The function of REM sleep and its relationship to dreaming:

The biological purpose of REM sleep is an enigma. A multitude of hypotheses, both biological and psychological, have been offered to explain the nature and purpose of REM sleep and dreaming. Several neurological functions of REM sleep have also been proposed, including:

(1) a neutralizing function, in counteractive relation to some noxious by-product of mammalian metabolism; (2) a

> stimulating function, in compensatory relation to the periodic sensory deprivation which is characteristic of mammalian sleep; (3) a reorganizing function, in response to the disorganizing effects of mammalian sleep on the central nervous system; (4) an alerting function, in preparation for mammalian fight and flight patterns; and (5) an innervating function, in the specific service of mammalian depth perception (Jones, 1970; pp. 167-168).

Crick & Mitchison (1983; 1986) have hypothesised that REM dreaming represents a process of neural "unlearning". According to these authors, superfluous neural network connections become activated in REM sleep and a honing or pruning process of these connections then occurs. This process is believed to enhance subsequent waking cognitive processes. Accordingly, when dreams are recalled, the process has presumably failed. It is therefore, according to this model, inadvisable to attempt to recall one's dreams. This hypothesis, however, lacks empirical support. Moreover, there is no evidence to date showing deleterious effects of dream recall. In fact, lack of dream recall is typical of neurological and psychiatric illnesses which impair memory, so that lack of recall might be indicative of a poor memory rather than an enhanced one as implied by Crick & Mitchison's theory. In addition, we have shown a positive correlation between dream recall and mood (discussed at length in Studies 1 and 2) suggesting that there may be

beneficial effects associated with dream recall.

Other evidence seems to support a possible role for REM in the enhancement of memory. For example, when subjects are shown movie excerpts prior to sleep, they show enhanced recall of these clips following REM compared to NREM, suggesting that REM enhances waking memory, at least temporarily (Reinsel & Antrobus, 1992).

Most people experience three to six REM periods per night yet recall few dreams. Apparently, during REM sleep consolidation of short term memory is impaired. Dream recall is enhanced considerably if an awakening directly follows REM sleep and if an effort to consciously think about the dream is made. Those who claim to "never" dream are assumed to have fewer awakenings from REM, and perhaps have less interest in their internal lives than are regular dream recallers.

> If patients suddenly remember more dreams than usual, either they now experience more awakenings or they have become more sensitized to internal psychological processes (Hauri, 1982, p. 19).

We tend to remember late morning dreams. Late morning dreams also tend to be those with the most regressive (i.e., the earliest of childhood memories) and most emotional psychological content (Kelly, 1985).

Several researchers have postulated that REM sleep might be instrumental to the regulation of mood and the cognitive processing of

affective experiences (Cartwright, 1986; Perlis & Nielsen, 1993; Kramer, 1993). This regulatory function is generally explained in psychological terms; however, REM sleep may be an endogenous mechanism that regulates neurochemical homeostasis (Hartmann, 1970), such that mood and well-being are a natural outcome of this balance. Hartmann (1973) theorizes that REM sleep restores mental functioning and psychological well-being that is otherwise depleted from waking trials and tribulations. This mental restoration is believed to be achieved through the restoration and homeostasis of catecholaminergic systems depleted in waking states.

In an older study, Gottschalk and colleagues have shown that anxiety levels in REM dreams are positively correlated with changes in free fatty acids. These authors suggest that the release of adrenaline and noradrenaline leads to increased fatty acid concentrations and, therefore, that anxiety in dreams is capable of triggering adrenergic discharge (Gottschalk, Stone, Gleser, et al., 1966).

In a more recent study, Gottschalk's group (Gottschalk, Buchsbaum, Gillin, et al., 1991) injected 10 normal male subjects with a glucose tracer during REM sleep. Localized cerebral glucose metabolic rates were measured by positron emission tomography (PET) and compared with level of anxiety in the corresponding dreams reported. They found a significant positive correlation between brain metabolic rates and dream anxiety levels in parietal and frontal cortexes.

Needless to say, the function of dreaming remains controversial. Yet, despite the apparent lack of understanding, we do know that dreams can have a profound impact on subsequent waking moods (Beauchemin & Hays, 1995; Beauchemin & Hays, 1996), and that selective deprivation of REM sleep can have drastic psychological consequences (Mendelson, 1987; Fiss, 1979). This, however, does not imply that the function of dreaming is purely psychological.

2.6.3 The differentiation between REM and NREM dreaming:

Since the original discovery of the REM sleep - dreaming correlate (Aserinsky & Kleitman, 1953), it has been discovered that dreaming, or at least active mentation, can and does take place outside of REM sleep (Foulkes, 1962; Ellman & Antrobus, 1992). When subjects are awakened from NREM sleep periods, they continue to report active mentation, leading many researchers to conclude that dreaming is not a distinctive feature of REM sleep. Although REM sleep nearly always involves a report of dreaming, NREM also appears to accommodates some form of mental activity. When a sleeping subject is awakened from REM sleep, 74 to 95% recall dreaming while reports from NREM range anywhere from 0 to 51% (Kelly, 1985).

Foulkes argues, at times quite convincingly, that NREM dreaming is both prevalent and indistinguisable from REM dreaming. He states that:

> Non-REM dreaming is not, as is still widely misunderstood, dreaming by some sort of special definition; many non-REM reports are dreams by anyone's definition of dreaming (Foulkes, 1996; p. 611).

However, it should be noted that this view of NREM dreaming has been as passionately challenged. Although studies reporting mentation outside of REM sleep are considered conclusive (Foulkes, 1962; Rechtschaffen, Verdone, & Wheaton, 1963), evidence suggests that the so called "dreams" reported outside of REM differ qualitatively from those experienced during REM sleep (Fiss, 1979). NREM dreams tend to be described as thought-like daydreaming while REM dreams are characteristically more bizarre and hallucinatory in nature (Kelly, 1985).

One of the main reasons for the vast discrepancies in findings here is perhaps a direct result of methodology. Studies that report high rates of recall for NREM dream reports tend to employ a fairly loose definition of dreaming. For example, upon being awakened from NREM sleep, subjects might be asked to report on "what was going through their mind". However, when subjects are ask to report more specifically on what they were "dreaming", reporting rates diminish substantially. Moreover, despite the mounting evidence for mentation in all stages of sleep, reports from REM sleep can be distinguished from Stage 2 NREM 92.5% of the time, on the basis of length of report alone (Antrobus, 1983). Moreover, Foulkes' (the

major proponent for the claim of NREM dreaming) studies may be criticised for possible experimenter bias. In the NREM sleep paradigm, subjects are usually awakened at the end of stage 2 sleep and asked to report mental activity. The end of stage 2 sleep is typically followed by an abrupt shift into REM sleep. Therefore, mentation reported here may be a reflection of upcoming REM that is yet detectible using crude EEG measurements. At the cellular level, REM sleep may have already commenced (McCarley, 1994).

Another view of NREM dreaming is that these dream reports might reflect a carry-over memory from an earlier REM period. However, Foulkes (1996) contends that NREM dream reports cannot solely be accounted for by recall from an earlier REM period, as dreaming reports have been collected from brief awakenings immediately following sleep onset when presumably no REM period has yet to occur. The debate goes on.

Differences in REM and NREM mental activity are apparently carried over into the waking state, at least temporarily. Reinsel & Antrobus (1992) report that differential carry-over effects on fantasy processes have been demonstrated upon awakening from various sleep stages. When subjects are asked to create stories using projective stimuli, responses following REM awakenings are longer, more visual, and more emotional than those given following NREM awakenings.

2.6.4 Dreaming and its physiological parallel:

McCarley (1983) postulates that there is an isomorphism between the physiological activity in REM sleep and the psychological experience of the dream. Successive REM periods of the night tend to increase in physiological intensity. This is somewhat paralleled by the intensity of dream content.

Hobson & McCarley (1977) proposed what they call the Activation Synthesis Hypothesis to explain the production of REM dreaming. They believe that the dream is, in essence, secondary to the physiological instigation (activation). Here non-cognitive information from the pons is relayed to the cerebral cortex where dream mentation is then produced to match the corresponding physiology (synthesis). While in the midst of dreaming, phasic activity occurs which, in turn, produces disruptions or shifts in the thematic dream sequences. This disruption process is said to account for corresponding level of bizarreness in the dream (Mamelak & Hobson, 1989).

2.6.5 Phasic REM activity:

A key difference between REM and NREM dreaming may be accounted for by phasic (in contrast to tonic) activity. Tonic activity is defined as the ongoing physiological state of REM, such as low-voltage -fast desynchronized EEG waves, whereas phasic activity refers to periodic events that wax and wane within the state, such as PGO waves and eye movements.

Ponto-geniculo-occipital (PGO) spikes or waves, measured by subcortical depth electrodes, herald the onset of REM. These waves continue to intermittently discharge throughout (Siegel, 1994). Although impossible to measure directly in humans because of the necessity of intrusive depth electrodes, PGO waves (or their analogue) are nevertheless assumed to be present in human sleep. In humans, phasic integrated potentials (PIPs) recorded from the eye muscles are believed to be a peripherally measured correlate of PGOs (Watson, 1992). PGO spikes (or their human equivalent) are tightly linked to REM sleep eye movements, which in humans are correspondingly linked to dream imagery. PIPs are associated with more bizarre and disorganized REM dream reports (Watson, 1992). Middle-ear muscle activity (MEMA) has also been suggested as a peripherally measurable indicator of PGO activity in humans. MEMA is also associated with corresponding dream bizarreness in REM reports (Watson, 1992).

Although the phasic events of REM sleep have been directly linked to the control of several brain stem sites:

> One must not view the rest of the brain as merely a passive responder to a REM sleep state generated in the pons. Instead, present evidence suggests a dynamic interaction between forebrain and other systems in moulding the structure and timing of PGO spikes and in all likelihood the dream imagery of REM

sleep (Seigel, 1994; p 134).

2.6.6 Laboratory versus home dream collection:

There is considerable debate over the most appropriate protocol for the study of dreams. Home retrospective dream recall studies, unlike those conducted in a structured laboratory setting, might be criticized for lacking structured experimental control. However, mounting evidence suggests that the home reporting method is much less intrusive and less affected by experimental biasing (Brown & Donderi, 1986). Even after several adaptation nights in a lab, dreams collected in this structured setting show diminished thematic, affective and social interactive aspects (Brown & Donderi, 1986), while home dreams contain fewer references to the experimental situation (Cohen, 1979). The disadvantage of home reporting is that the physiological correlates of dreaming cannot easily be measured, and recall is diminished in retrospective reporting. The appropriate protocol is dictated by the underlying purpose of the study (Kramer, 1994). Essentially, both methods are valid; both have inherent problems.

2.6.7 Dream recall and methodological considerations:

When the focus of research is the content of dreams, it is implicitly imparted and now explicitly stated, that these are the *dreams recalled* rather than the actual *dreams experienced*. This is an important distinction

because: (1) some distortion in reporting will necessarily occur in retrospective reporting as memory is a reconstructive process (Wade & Travis, 1996) , and (2) very few of the actual dreams experienced nightly will be recalled. Given the ephemeral nature of dreams, it is likely that the longer the delay between the time of report and the actual experience, the greater the distortion in reporting will be.

A major critisism of dream-content studies is the reliance on self-report. Beyond the problem of accurate memory reconstruction limitations, elaborate embellishment or confabulation may occur. If an accurate measure of actual experience is of necessity, then dream content research is untenable as a scientific pursuit. However, in the studies of dream content reported in this thesis, the relationship between dream content and mood might more accurately be discribed as: the relationship between the subject's account of an experience and the subject's account of his or her mood. If this relationship is significant, then the actual experience, which can never be known, is in some respects ineffable. An analogous situation to this might be the relationship between schizophrenia and reports of auditory hallucinations. We cannot measure or detect auditory traces of these voices, and whether or not they are true experiences is not an issue. Instead, what is important is the fact that they are reported.

Normal recall in non-laboratory retrospective dream reporting averages about 2 to 3 dreams per week. This is likely to be a mere fraction of

the actual dreams experienced, given that the average person has 4-5 REM periods per night, where dreaming inevitably occurs. In addition, other NREM mentation is also occurring a great percentage of the time in sleep. A person can conceivably experience a dozen or more dreams per night but recall very few or none at all.

Although some people claim to recall many dreams per night, still others insist that they "never dream". Yet, "never dream" subjects can, in fact, be shown to be otherwise when awakened after REM periods in a laboratory. The failure to recall dreams does not imply that less dreaming is actually occurring, but rather that less retrieval is available (Goldmann, 1990). Dreams are best remembered when the sleeper is awakened during or shortly following the dream experience where memory consolidation is believed to take place (Rosenblatt, Antrobus, & Zimler, 1992).

Several factors have been suggested to account for individual differences in dream recall, such as:

> how a subject is awakened; the setting of the awakening; the motivation; personality; and cognitive style of the subject; the demand characteristics of the interviewer; and the characteristics of the dream itself (Goldmann, 1990; p. 131).

It has been suggested that the nature of the questioning also greatly influences the dream report (Herman, 1992). Demand characteristics are

certainly influential if not properly controlled for in any experimental design, particularly one in which a subjective report is relied upon. However, subjects' motivation to accurately report might be underestimated. When a deliberate attempt was made to bias elicited dream reports, subjects showed active attempts to resist the experimenter's attempts to manipulate the reports (Roffwarg, Herman, Bow-Anders & Tauber, 1978).

2.6.8 The content of 'normal' dreams:

What factors determine the content of our dreams? Kramer, Roth, and Palmer (1976) say that the content of our dreams reflects a continuity with waking thought. These authors compared REM dream reports to waking fantasy and personality measures and found that the dream reports reflected strong positive correlations with waking thought and feeling measures. Rados and Cartwright (1982) claim that dream content is more predictable from pre-sleep ideation and spontaneously occurring mentation than from direct inquiries about recent and significant problems and concerns. In light of these findings, it is not surprising that the dreams of the depressed might reflect a negative cognitive schema.

However, these findings have been challenged. Some researchers claim that pre-sleep ideation does not successfully predict REM dream content. This challenge was based on a large number of subjects who were asked to report on pre-sleep ideation and who were subsequently awakened

from REM sleep and asked to report on dream content (Roussy, Camirand, Mercier, et al., 1995). This discrepancy might be accounted for by divergent methodologies. In the above study, subjects reported dreams from only the first REM period. Although there is some thematic dream continuity across the night, dreams from the later part of sleep tend to become more lengthy, regressive, and emotionally laden (Kelly, 1985). Therefore, it may be that dreams collected in different REM periods nightly might reflect different aspects of the person's waking state. Moreover, dreams reported from spontaneous home recall may be selectively remembered and reported based on one's waking concerns.

2.7 MOOD DISORDERS

It would be an over generalization to say that all "depressed" people sleep or dream in a particular way. This is because the word "depression" is used generically to describe an enormous range of affect, from the lay definition of "the blues" to extreme clinical cases of psychomotor catatonia. Therefore, a definitive overview of the relationship between sleep, dreaming and depression becomes possible only when attention is paid to the nosology or classification of mood disorders. For this reason, I will first present a brief overview of the classification of mood disorders, so that subsequent reports can be understood in their proper context.

2.7.1 Classification of mood disorders:

The Revised Diagnostic and Statistical Manual (DSM-IV) of the American Psychiatric Association (1994) is one of the main diagnostic guides used in psychiatry. All psychiatric disorders are classified in a multi-axial mode and are considered either primary or secondary in nature. If a disorder is primary, it is the most prominent and pervasive symptom or cluster of symptoms presented. Sometimes, this primary diagnosis can also be accompanied by a secondary one, a less prominent and perhaps related symptom or set of symptoms. For example, depression is often found in secondary association with other disorders such as Schizophrenia, Sleep Disorders, Organic Mental Syndromes, Psychoactive Substance Abuse Disorders and Uncomplicated Bereavement (Davison & Neale, 1990). In these instances, the depression is thought to be associated with, or an offshoot of, the first problem. All the research presented in this thesis will focus on mood disorders as a primary diagnosis unless otherwise noted. In particular, the focus will be on Bipolar Disorder (BD); although, in light of its relevance, a review of Major Depressive Disorder (MDD) in relation to sleep will also be considered.

2.7.2 Major Depressive Disorder:

Major Depressive Disorder (or unipolar depression) is a term used to describe a profound episode of mood disturbance that leads to social or

occupational impairment. It is characterized by the presence of a group of symptoms, five or more of which must be present for a period exceeding two weeks. These include: (1) depressed mood, (2) diminished interest or pleasure in previously pleasurable experiences (anhedonia), (3) significant appetite or weight change, (4) insomnia or hypersomnia, (5) psychomotor agitation or retardation, (6) fatigue or loss of energy and libido, (7) feeling of guilt and worthlessness, (8) diminished concentration and indecisiveness, and (9) preoccupation with death and suicidal ideation. In addition, these symptoms must not be accounted for by pharmacological or organic factors and must not be the direct expression of a bereavement (American Psychiatric Association, 1994).

2.7.3 Bipolar Disorder:

The essential feature of bipolar disorder (still often referred to as Manic-Depression) is the occurrence of one or more manic, or hypomanic episodes typically associated with one or more depressive episodes. It is generally characterized by periodic fluctuations between extreme mood states (Georgogotas, 1988). Bipolar disorder is further sub-classified as either manic, depressed or mixed, according to the most recent or prevailing symptoms. Clinical features of bipolar disorder include such things as mood lability, and slow or rapid shifting between elevated, agitated, or depressed mood. Episodes of mood disturbances can last moments, days, or months.

Sometimes episodes follow a cyclical pattern of occurrence.

2.7.4 Mania:

Mania refers to a distinct period of elation frequently accompanied by such symptoms as: increased psychomotor activity, increased pressure and rate of speech, heightened irritability and aggressive behaviour, hyper-sexuality, decreased need for sleep, increased risk-taking behaviours, distractibility, flights of idea, and a sense of grandiosity (Goodwin & Redfield Jamison, 1990). Delusions and hallucinations can be present but tend to remain mood congruent. In mania, these symptom are extreme, such that they are considered psychotic and almost always result in social impairment or adverse social consequences and usually require hospitalization.

2.7.5 Hypomania:

In hypomania, symptoms are similar to those of mania but are more moderate. Hypomania is a mild state of mania and can sometimes facilitate great accomplishment due to increased drive, energy, and creativity. Mood in hypomania is usually exuberant, jovial and self confident, but at times with an underpinning of agitation or irritation (Goodwin & Redfield Jamison, 1990) and an easily triggered outburst of anger. Energy level is high and the person tends to be very social, gregarious, and talkative. There is no firm

differentiation between mania and hypomania as they reflect a difference in degree and not in kind. Sometimes these terms are used interchangeably. However, generally speaking mania is always severely pathological and psychotic while hypomania is considered a milder form of psychosis.

2.7.6 Mixed states:

Mixed mood states often prevail in bipolar disorder. In mixed states, a combination of depressed and manic symptoms are simultaneously displayed. For example, a patient may rave about his or her important accomplishments, and at the same time, entertain suicidal thoughts. The symptomatic presentation of mixed states has been characterized as the presence of dysphoric mood, alternating with euphoria, grandiosity, racing thoughts, suicidal ideation, persecutory delusions, hyper-sexuality and insomnia (Goodwin & Redfield Jamison, 1990).

2.7.7 Depressed states:

In depressed states, bipolar patients often become despondent, sad, weepy, lethargic and pessimistic. Suicidal preoccupations and outright attempts are not uncommon. Although the symptoms of the depressed stage of bipolar disorder resemble those of a unipolar (MDD) depression, there tend to be some distinguishing characteristics. For example, hypersomnolence is more common in the former, and early morning insomnia for the latter. Also,

weight loss is more often found in association with unipolar depressions, whereas weight gain is sometimes seen in bipolar depressions.

2.7.8 Seasonal Affective Disorder:

Seasonal Affective Disorder (SAD) consists of repeated mild to moderate winter depression with ancillary symptoms of hypersomnia, carbohydrate cravings, weight gain, irritability and a period of elevated mood in the spring (Rosenthal, Sack, Gillin, et al., 1984). SAD has been described as a chrononbiological disorder. However, there is a lingering debate about the status of SAD as an illness; some have argued that it is a sub-clinical phenomenon - "the winter blues". Others have proposed that SAD might be a variant of bipolar disorder with a seasonal component (Monk, 1993).

Alongside the discovery of SAD was the interesting discovery that nocturnal secretion of the pineal hormone melatonin could be suppressed by high levels of bright artificial light (Lewy, Wehr, Goodwin, et al., 1980). This led to both a treatment strategy and, in and of itself, lent credence to the disorder of SAD. The effects of light on mood, sleep, and chronobiology will be discussed at length under a subsequent heading.

2.7.9 Epidemiology of mood disorders:

Mood disorders are the most prevalent of psychiatric disorders (Kaplan & Sadock, 1991). Estimates of lifetime prevalence rates for all mood

disorders is 8.3%. Females have a much higher preponderance of unipolar depression (a ratio usually reported as 3:1). The prevalence of bipolar disorder appears to be more equally distributed in terms of gender, i.e., males and females are equally afflicted (Regier, Boyd, Burke, et al., 1988).

The origins of bipolar disorder (and unipolar MDD) may be multiple, that is, arising from no one single isolated cause. However, perhaps more than any other common psychiatric disorder, bipolar disorder has a strong genetic heritability component. The concordance rate for monozygotic twins is 79%, in contrast to 24 % for dizygotic twins. Unipolar concordance rates are 54% and 19% respectively (Regier, Boyd, Burke, et al., 1988). Still, epidemiological studies show that numerous environmental factors are significantly prevalent in the backgrounds of both types of depressives; a common factor being the experience of an early loss particularly in BD (Kaplan & Sadock, 1991): interestingly, a finding consistent with early Freudian theory. Freud (1916) suspected that complicated bereavement led to melancholia. The diathesis-stress model of psychopathology asserts that there is an interaction between a predisposition towards disease (the diathesis) and environmental, or life events (stress) (Davison & Neale, 1990) such that biology affects behaviour and the environment, and environment and behaviour, in turn, affect biology. This is the model adopted here.

2.8 SLEEP AND AFFECTIVE DISORDERS

In a recent meta-analysis of sleep and psychiatric disorders, Benca and her colleagues concluded that the sleep of affective disordered patients differed most frequently and most significantly from any other class of psychiatric disorders when compared to normal controls (Benca, Obermeyer, Thisted & Gillin, 1992).

2.8.1 Sleep and bipolar disorder

In a longitudinal study of bipolar patients, Hartmann (1968a) found that in the depressed phase of bipolar disorder, total sleep time was higher than during controlled periods. Overall REM sleep time was also increased during depressed phases, particularly in the more severely depressed.

In manic or hypomanic phases of bipolar disorder, the relative time spent in both sleep and REM sleep is said to diminish drastically (Hartmann, 1968b). Moreover, a reduction in sleep (spontaneously occurring or deliberately enforced) appears to precipitate switching to mania. According to Wehr's group: " many of the diverse psychological, interpersonal, environmental, and pharmacological factors that appear to trigger the onset of mania could do so through their capacity to cause sleep deprivation (Wehr, Sack, & Rosenthal, 1987; p 201)." Partial or total sleep deprivation for one night has been shown to induce transient or sustained switches into mania or hypomania in bipolar patients. When Wehr et al.,

(1987) deprived 12 bipolar patients of total sleep for one night, 75% switched into a state of mania or hypomania that night or the following day. Six patients remained manic for several days, while 3 returned to depression after recovery sleep.

In an EEG sleep study of manic patients, Hudson, Lipinski, Frankenburg, et al., (1988) report that manic patients exhibited significantly decreased total sleep, along with increased time awake, particularly in the last 2 hours of the recording night. Manic bipolar patients also exhibited a shortened latency to REM sleep with increased REM activity and density. The authors conclude that mania is associated with marked disturbances of sleep continuity and REM sleep measures. However, the claim of a reduced REM sleep latency in mania was not supported in our study (Beauchemin & Hays, 1996) which is reported in detail in study 2.
Moreover, although a reduction in sleep appears to promote a switch to mania, our findings suggest that events within sleep itself, namely dreaming, might also contribute to this switch.

Sleep architecture has also been reported as abnormal in the depressed phase of bipolar disorder (Thase, Himmelhoch, Mallinger, et al., 1989). Findings include poor sleep continuity, and lowered amount of stage 1, 3 and 4 delta slow wave sleep (SWS). While Thase et al., (1989) and others (Jernajczyk, 1979) did not find a reduced REM sleep latency in bipolar depression, others have reported this phenomena (Duncan, Pettigrew &

Gillin, 1979; Beauchemin & Hays, 1996).

2.8.2 REM sleep and unipolar depression

Several anomalous characteristics in sleep are prevalent in unipolar depression, including an abnormal temporal distribution of REM sleep (Vogel, Vogel, McBee, et al., 1980), with overproduction of REM sleep in the first third of the sleep cycle (Van den Hoofdakker, Beersma & Dijk, 1986). In depressed subjects, there is a tendency for an increased amount of early REM sleep, in both quantity and intensity. This early clustering (Hauri & Hawkins, 1971; Kupfer, Ehlers, & Frank, et al., 1991) is in contrast to the expanding progression of REM periods seen in normal subjects.

2.8.3 Reduced REM sleep latency:

By far the most pervasive finding in the sleep of depressives is a tendency for an earlier onset of the first REM episode (reduced REM latency) (Kupfer, 1984a; Kupfer, 1984b). Thus, the usual latency period (about 90 minutes) is often grossly shortened in sleep recordings of the depressed (Coble, Kupfer & Shaw, 1981). A reduced latency and early clustering of REM sleep suggests that the neural control mechanisms of REM sleep might somehow be defective. As these sleep abnormalities occur in conjunction with depression, it is assumed that the mechanism(s) that control REM sleep might also contribute to, or cause the comorbid depression (McCarley, 1982).

In other words, an imbalance in either the neurochemicals that generate REM sleep, or those that "turn it off", might lead to depression. It is also possible that both are caused by some unknown third variable.

An alternative explanation is derived from a chronobiological perspective.

2.8.4 Chronobiological abnormalities in depression:

A competing explanation for the alteration in REM sleep in depressives comes from chronobiologists. A "desynchronization hypothesis" was postulated and asserts that there are two or more circadian processes which diverge and run at different rates due to lack of internal entrainment of one or more of these oscillators to daily environmental cycles (Monk, 1993). Although certain rapid-cycling bipolar patients do show evidence of circadian desynchrony, a free-running study of depressive patients fails to support this hypothesis (Wehr, Sack, Duncan, et al., 1985).

A reduced REM sleep latency may be more specifically accounted for by a phase-advanced anomaly in circadian rhythm. This hypothesis is supported by findings of altered diurnal temperatures (Benca, 1994) and cortisol secretion advances (Linkowski, Mendlewicz, Leclercq, et al., 1985), both of which are taken as measures of circadian pattern (Benca, 1994). A positive phase advance of the temperature curve has been reported in some depressive patients (Avery, Wildschiodtz, & Rafsaelsen, 1982). The

underlying assumption of this model is that the circadian oscillator governing REM sleep is advanced relative to the sleep-wake cycle (Benca, 1994). Weitzman's group described a parallel between sleep in subjects who had undergone an acute 12 hour phase shift. These subjects subsequently experienced shortened REM sleep latencies, increased wakefulness, and increased early night REM sleep (Weitzman & Kripke, 1981), all characteristics of the sleep of unipolar depressives.

Additional support for this theory comes from the finding that sleep deprivation is ameliorative to depressives (Vogel, 1975) but not normals. Although there are alternative explanations as to why sleep deprivation may be of therapeutic significance, a chronobiological account attributes amelioration to a resynchronization process which results from partial sleep deprivation.

2.8.5 Neurochemical theories of sleep and depression:

Several interacting neurotransmitters are presumed to regulate REM sleep. These include primarily: acetylcholine (ACh), serotonin (5-HT), and noradrenaline (NA) (Kelly, 1985). In Hobson's "Reciprocal Interaction Model" (RI), it is postulated that there is an antagonistic relationship between the excitatory ACh neurons in the pontine reticular formation and inhibitory mono-aminergic neurons: 5-HT in the raphe nuclei and NA in the locus ceruleus (Hobson, 1990; Hobson, 1988; McCarley, 1982). REM sleep activity

is believed to occur when the cholinoceptive pontine reticular system escapes inhibition during reduced monoaminergic levels (Hobson, 1988). These two systems are thought to interact in an oscillating manner throughout the night, generating, and then subsequently inhibiting, REM sleep episodes (McCarley, 1982). "Thus the sensitive zone appears to be a point of convergence of the neurons postulated to interact reciprocally in order to generate the NREM-REM sleep cycle (Hobson, 1990; p.378)".

Neuropharmacological studies confirm that cholinergic activity in the medial pontine reticular formation (PRF) is responsible for the generation of REM sleep (Baghdoyan, Rodrigo-Angulo, McCarley, et al., 1984; Hobson, 1988). Direct infusion of several cholinergic agonists into the brainstem PRF of animals has been shown to evoke REM activity, with increased cortical desynchronization, reduced REM latency and increased duration of REM periods (McCarley, 1982). Moreover, the artificial cholinergic induction of REM sleep appears to be site specific in the PRF, as injections into adjacent brainstem sites do not result in REM production (Baghdoyan et al., 1984).

When human subjects are given cholinergic agonists by intravenous injection during the NREM cycle, REM sleep quickly ensues (Hobson, 1990). In remitted bipolar patients, arecoline administered after the first REM episode results in significantly reduced latencies to second REM sleep episode and higher REM percentages and densities (Sitaram, Nurnberger, Gershon, et al., 1982). Thus, support for the specificity of cholinergic

mediation of REM sleep appears robust; however, whether cholinergic activity also underlies clinical depression is less clear. Sitaram and colleagues (1982) have interpreted the tendency for an increased responsiveness to artificial REM induction in bipolar patients as evidence of a muscarinic receptor sensitivity in affective disorders. However, it is not clear as to whether this difference (reduced 2nd REM latency) exists independently of cholinergic provocation. Reduced REM latencies to the first or subsequent REM periods may be the consequence of a failure of the REM inhibition mechanisms (presumably NA & 5-HT) rather than a sensitivity to REM induction.

ACh does not appear to be a causal agent of depression, nor does there appear to be consistent evidence for an overall increased amount of REM sleep during depression (Hartmann, 1970); rather, the tendency is for REM sleep to be prematurely dense and its temporal distribution to be anomalous (Vogel et al., 1980). This suggests that overall ACh levels are not necessarily elevated but perhaps not adequately suppressed or gated. Given the propensity for an early clustering of REM sleep, we might expect ACh levels to be highest in the early evening but lowest in late morning sleep when REM sleep tends to be lowest (in depressives). If ACh caused depression, mood and ACh levels should then be inversely related, i.e., the higher the ACh levels, the lower the mood. Yet most patients with affective disorders report their lowest mood in the morning (Beck, 1970), a time when

presumably ACh levels are lowest. Furthermore, there is no evidence to suggest that anticholinergic drugs alone are effective antidepressants (Govoni & Hayes, 1988). Most older antidepressants do have some anticholinergic effects but the newer SSRIs do not.

Taken together, these findings suggest that the putative "REM off" mechanism, NA and 5-HT, might be implicated in both the lack of REM sleep inhibition, and the corresponding depression. If, as proposed by Hobson and McCarley (Hobson, McCarley & Wyzinski, 1975; McCarley, 1982), the monoaminergic system functions as the gating mechanism for REM sleep, a relative decrease in 5-HT or NA would logically result in a premature discharge of REM activity by failure of inhibition. Evidence suggests that this is the case. Blocking noradrenergic activity with popranolol, a β-blocker, does increase REM sleep (McCarley, 1982) and cause depressive-like symptoms (van Praag, 1981). However, this "disinhibition" of REM may not be an exclusive result of monoamine blockade in the locus ceruleus (LC), as bilateral lesions in the LC fail to demonstrate notable effects on sleep (Jones, Harper, & Halaris, 1977). Moreover, lesions, or complete destruction of the gigantocellular tegmental field (FTG) failed to abolish REM sleep (Hobson, Lydic & Baghdoyan, 1986). These criticisms have prompted Hobson and colleagues to revise their reciprocal-interaction (RI) model of sleep somewhat. The idea that the sleep cycle is generated by the specific interaction of highly localized neuronal activity has been revised by the view that these cycles

may involve a more complex and dynamic interaction between multiple anatomically distributed neurons (Hobson, Lydic & Baghdoyan, 1986).

2.9 ANTIDEPRESSANT DRUGS AND SLEEP

Virtually all classes of antidepressant drugs have immediate and profound effects on sleep, irrespective of their mode of action (Nicholson, Bradley, & Pascoe, 1994) although these effects are not always enduring. In particular, most antidepressants tend to suppress and delay the onset of REM sleep (Benca, 1994). Reduction in REM sleep follows treatment with tricyclics such as amitriptyline, nortriptyline, and desipramine; mono-amine-oxidase inhibitors (MAOIs): clorgyline and pargyline; and to a lessor degree with selective-serotonin reuptake inhibitors such as fluoxetine (Sharpley & Cowen, 1995). There is evidence that, by the mechanism of tolerance, REM sleep escapes from suppression (Nicholson, Bradley, & Pascoe, 1994).

The greatest inhibition of REM sleep is seen with the older tricyclics. For example, in one experimental study, when cats were given imipramine their REM sleep was found to be almost completely suppressed (Kramer, Whitman, Baldridge, et al, 1968). Clonidine, a potent and specific alpha-adrenergic partial agonist causes drastic suppression of REM sleep at very low doses. However, when clonidine was administered intravenously to depressives during their second NREM sleep period, these subjects showed significantly less REM suppressant effects compared to normal controls

(Schittecatte et al., 1992). On the basis of their findings, these authors conclude that results are consistent with and support the cholinergic-aminergic imbalance hypothesis of depression. This hypothesis suggests that depression, along with its pervasive sleep abnormalities, is caused by increased cholinergic activity (as supported by the findings of muscarinic supersensitivity) and decreased adrenergic activity caused by downregulation (Schittecatte, et al., 1992).

However, other mechanisms may underlie both depression and its concomitant sleep abnormalities. One report states that a subset of depressed patients with typical clinical and polysomnographic abnormalities had a complete and rapid reversal of depression and a normalization of sleep following administration of pindolel, a dopamine agonist (Kapur & Mann, 1987).

Lithium, which is used primarily as a mood stabilizer in bipolar disorder, is also associated with a partial suppression of REM sleep and REM latency and an increase in SWS, although reports are equivocal. It would appear that lithium's effects on sleep are generally minor relative to other drugs. Sleep effects are even less detectable in normals given lithium, making it difficult to separate drug effects from direct effect of the disorder (Nicholson, Bradley, & Pascoe, 1994). Moreover, lithium's neurochemical effects are rather widespread and non-specific (Bunney, Blynn, & Garland-Bunney, 1987) making it difficult to draw inferences between specific

neurochemical changes and sleep alternations. In addition, circumstantial evidence for the phase advance hypothesis comes from the finding that many antidepressants, including lithium, MAO inhibitors and tricyclics, have demonstrated a lengthening effect on circadian rhythm (Wirz-Justice, 1983).

Trimipramine and nefazadone represent some of the few documented antidepressants that do not suppress REM sleep. When human subjects' REM sleep was monitored following regular doses of trimipramine, they reported more frequent and more pleasant episodes of dreaming. Conversely, pharmacologically naive controls reported short, trivial and passive dreams more typically associated with depression (Riemann, Low, Schredl, et al, 1990).

There are some anecdotal claims that SSRIs, and in particular, fluoxetine, increases vividness and intensity of recalled dreams. In a recent letter to the editor, one clinician reported that four patients being treated with fluoxetine described an intensification of dreaming. Fluoxetine was reported as bringing "colour and excitement into the perceived drabness of their dreams (Markowitz, 1991; p. 432)." This was apparently not just a function of recovery, as the dreams were said to have returned to baseline upon discontinuing the drug. Bupropion, a less common and novel antidepressant drug with dopaminergic properties, is also reported to cause a perceptual intensification of dream imagery (Becker & Dufresne, 1982).

Nightmares can also be a side effect of some antidepressants, although

they are more likely following treatment with dopamine agonists, cholinergics, and beta-adrenergic blockers (Hartmann, 1984). Withdrawal from barbiturates, benzodiazepines, and alcohol is also associated with more vivid, bizarre dreams and nightmares. In these cases, the dream intensification phenomenon is likely to be generated by a rebound of REM which follows its suppression. A partial REM rebound, i.e., a tendency to delay REM sleep until later in the night, may underlie some of the intensification phenomenon reported with SSRIs and other antidepressants.

2.10 LIGHT: EFFECTS ON MOOD AND CIRCADIAN RHYTHM

Bright light treatment is now used routinely for the treatment of Seasonal -Affective-Disorder (SAD), which has been described in detail in section 2.7. Treatment consists of sitting, with eyes open, close to a bright lamp designed to emit a high level of fluorescent illumination (usually 10,000 lux). Generally this is done for a period of 1/2 to 2 hours per day. There is some debate as to the most effective timing; however, it is generally considered most effective in the early morning. Some proponents have argued for phase-typing of patients (Lewy, Sack & Singer, 1985). According to this method, those showing an advanced circadian rhythm (phase-advance) should preferentially respond to late afternoon light, while those having a delayed circadian rhythm (phase-delay) should respond best to morning light. This premise is based on findings showing that bright light in

the morning phase advances circadian rhythm, whereas evening light has a delaying effect on circadian rhythm. The underlying assumption, then, is that chrononbiologic disorders of mood and sleep can be treated by normalizing circadian synchrony. However, while this is likely the case for jet-lag and shift work syndromes, it is less clear in relation to mood disorders.

Light's mechanism of action remains largely unknown. There is evidence suggesting that light suppresses secretion of pineal melatonin (Lewy et al., 1980), which is directly implicated in modulation of circadian rhythm and hence of sleep. Circadian desynchronization may underlie the pathogenesis of mood disorders. However, there is no clear evidence for melatonin secretion abnormalities in SAD (Lam, Kripke & Gillin, 1989) but apparently melatonin administration exacerbates symptoms in depressives (Carmen, Post, Buswell, et al., 1976). Also, a hypothetical low melatonin syndrome in depression has been proposed by Beck-Friis and colleagues (Beck-Friis, Kjellmen, Aperia, et al., 1985). Interestingly, these researcher found that depressed patients who reported parental loss before age 17 had subnormal melatonin levels compared to those with no history of loss. The issue of loss was touched upon in the discussion of depression and will again be discussed in the final discussion section as it pertains to the reported studies.

Given the connection between circadian rhythm, sleep, and melatonin and the fact that light inhibits melatonin secretion, one would anticipate an

effect (at least indirectly) of light on sleep. Anecdotal improvement in sleep is often reported following light therapy; however, this is generally based on patients' subjective assessments of sleep quality. In one trial with SAD patients, no measurable changes in sleep recordings were observed following light treatment (Partonen, Appelburg, & Partinen, 1993). It would appear on the basis of this findings that improvement in mood is not directly attributable to measurable changes in sleep. However, this is but a preliminary assumption that requires replication. It is also unknown at this point as to whether these findings can be generalized to other mood disorders. This question is addressed in Study 4 (see chapter 6).

Sleep is not usually measured as a dependant variable in studies that employ light-therapy specifically for mood. It usually only commands attention as a dependant variable when the goal is circadian rhythm phase-shifting, such as in the study of light treatment for shift-work problems and jet-lag.

If sleep is not directly altered by light, then an alternative explanation (beyond melatonin suppression) for the effect of light on mood is required. A possible alternate mechanism of action may be related to the neurochemical serotonin (5-HT). Low brain levels of serotonin is one accepted causal theory of depression and increased blood levels of serotonin have been reported following exposure to bright light (Rao, Muller-Oerlinghausen, Mackert, et al., 1990). However, there is no evidence that

increased serotonin levels can cause mania, even though exposure to bright-light can, and often does. This suggests that some other neurchemical change(s) might result from bright light exposure, such as increased dopamine, noradrenaline, or endorphin, all of which have some hypothesized (albeit tentative) relationship to depression .

Despite the above mentioned possibilities, the mechanism of action of light-therapy remains in question. Many have suggested that improvements in mood might be solely attributable to placebo effect as some studies report no effects (Levitt, Wesson, Joffe, et al., 1996) and others argue that no appropriate control group can be established (Carrier & Dumont, 1994). A true controlled experiment for light-therapy is hard to conceive. If a no-light treatment is used as a control group, then participants are not "blind" to group assignment nor do they receive the same experimental treatment. Therefore, most trials use low-light for a control group, despite reports of placebo effects for even very low intensities of light. Despite these difficulties, any treatment which may be beneficial, especially one with negligible side effects, is worth assessing for efficacy. Moreover, despite lingering scepticism and conflicting reports, bright light continues to be the conventional treatment for SAD and is said to also ameliorate nonseasonal unipolor (Peter, Rabiger, & Kowilak, 1986; Kripke et al., 1987; Kripke et al., 1992), and bipolar depressions (Papatheodorou & Kutcher, 1995).

In attempt to further elucidate this somewhat controversial matter, we

conducted a trial of efficacy for light therapy as an adjuvant to pharmacotherapy. This also conveniently supplied us with a means of artificial rapid mood change induction so that we could simultaneously study sleep in relation to mood in bipolar disordered patients. We planned to use intensities above what has generally been reported. We used two groups, one receiving bright light and the other light of lesser intensity. The goal was to ensure that all patients experienced rapid mood improvement. This would facilitate the dream-sleep study (Study 2) and at the same time, accommodate the search for a differential response between high and low light groups. This work is discussed in detail in Study 3.

2.11 DREAMING AND MOOD DISORDERS

2.11.1 Dreaming and depression:

The manifest content of depressives' dreams has been described as prosaic and lacking in emotional content or as short and mundane (Riemann et al., 1990; Van de Castle & Hollaway, 1990; Beauchemin & Hays, 1995). Other have reported that depressives' dreams focus more on family members (Langs, 1966; Kramer et al., 1968), or portray the dreamer as victimized (a type of dream known as masochistic) (Beck & Ward, 1961). Themes of helplessness and hopelessness are significantly more common in depressives than in controls (Whitman, Kramer, Ornstein, et al., 1970). Cartwright (1992) reports that women, whether depressed or not, reported more dreams

of a "masochistic" theme. She concludes that:

> dreaming of being subjected to negative events and/or negative self-definitions appears to be a continuing trait more characteristic of women then men. This tendency becomes exacerbated during a depressive episode (p. 79).

Riemann et al. (1990), recently reported that depressed inpatients did not reveal a high level of "masochistic" dreams in a laboratory dream collection study. Rather, they reported a marked brevity or absence of dream reports and of those reported, all were described as rather mundane.

Miller (1969) once suggested that the dreams of the severely depressed are pleasant, and lacking in conflict. He accounts for this apparent contradiction by attributing differences in dream themes to the corresponding depth of depression. He suggests that while the dreams of the severely depressed are pleasant and prosaic, their dreams during recovery tend to show more strife.

Thus, although several studies have reported a tendency for "masochism" in depressives' dreams, this is a questionable conclusion because: (1) findings are not consistent; (2) control subjects were not always used for comparison, (3) individual and perhaps gender differences may outweigh group differences. A more consistent finding is that depressive either report brief and uneventful dreams or recall no dreams at all.

Although it may at first sight appear to be the case, there is no evidence to suggest that *less* dreaming occurs during depression. In fact, some studies report more overall REM sleep time (Hartmann, 1970) which, at least indirectly, might translate to an increase in dreaming. It is possible that the "barren" dream narratives during depression may be a function of reporting style that is itself influenced by the depression. "The brevity of the dream reported by depressed patients may be related more to their psychomotor retardation than to the [actual] length of their dream experience (Kramer, 1991a; p.150)." Severely depressed patients often experience memory problem in general so this probably influences dream recall as well (Riemann et al., 1990). One study tested this assumption and reported that depressed subjects also showed a diminished ability to report waking fantasies (Whitman et al., 1970). These authors concluded that, although depressed subjects dreamt as much as non-depressed subjects, they were unable to report these dreams in detail.

Another explanation for barren dreams may be related to changes in the corresponding phasic activity in REM sleep such as decreased eye movement density (Oswald, Berger, Jaramillo, et al., 1963). However, REM density (a measure of eye movement activity) is more consistently reported as increased during depression and not decreased. One explanation for this discrepancy may be related to the actual distribution of REM sleep in depression which tends to be pathologically clustered and dense in the first

half of the night. The likelihood of remembering a dream is very low if it is not followed by awakening. Thus, temporal relationship to awakening (early night dreaming) may account for a lack of dream recall in depressives.

Improvement in depression has been correlated with changes in dream content, reporting frequency, and affective tone (Kramer, 1991a). Riemann et al., (1990) found that antidepressive treatment with trimipramine had a positive influence on patient's mood that corresponded to positive mood changes within their dream content. Kramer et al., (Kramer, Sandler, Whitman, et al., 1970) found that following treatment with antidepressants, the emotional content in male dreams increased. In females, social interaction themes decreased and activity levels increased.

Kramer (1991b) writes that:

> Dream content is clearly altered in the severely depressed .... The dreams of the depressed may be characterized as shorter, barren, and containing more family members as the unique character type.... The dreams of the depressed change in response to improvement in the depressive condition of the patient. With improvement, the dreams become less hostile and show more intimacy, heterosexuality and motility (p. 179).

The aforementioned studies focus mainly on the dreams of "primary

endogenous unipolar depressives". Therefore, determining whether these dreams are also representative of the depressed stage of bipolar disorder was, in part, a goal of Study 2.

2.11.2 Dreaming and bipolar disorder:

Prevailing mood state (i.e., depression and mania) and the transition between these states appear to be related to changes in sleep and dreaming in bipolar disorder. Changes in sleep patterns are often noted at transition points between mood states. Stressful occurrences often precipitate a mood shift (Goodwin & Redfield Jamison, 1990). Many known precipitating factors leading to mania also interfere with sleep (Wehr et al., 1987). It has also been noted that shifts, particularly from depression to mania, frequently occur in sleep (Hartmann, 1989).

Hartmann (1968b) claims to:

> have found not a single case in which a sudden shift to mania clearly occurred during waking. [He states that] although the exact mechanisms are, of course unknown; it may be that an actual dream during the night is involved in initiating the change (p. 327).

As stress is a known precipitant of a switch to mania, it may be that a stressful event in sleep, perhaps a dream itself, may underlie mood-cycling. Levitan (1977) appears to support this hypothesis, writing that:

> the sudden abrogation of the traumatic situation in the dream seem[s] to be a critical moment in which the stage [is] set for the emergence of [the factors] responsible for the creation of mania (p. 146).

These claims fostered my original hypothesis that a particular type of stressful dream might herald an upcoming mood shift. This was also, in part, supported by others' clinical observations of the dreams of bipolar patients; however, reports tended to be anecdotal, involving single cases. For example, Stone (1978) noted one bipolar patient had "stark dreams of fragmentation of the body" just prior to a shift from depression to a manic psychosis. Another patient was said to have reported a recurrent dream of being painlessly "burned at the stake" that preceded and continued throughout her manic episodes (Pao, cited in Levitan, 1977).

Stone (1978) notes that several subtle changes can alert a clinician to an oncoming state of mania, including:

> ... insensitivity to the feelings of others, intensity, ambitiousness, explosive temper, overfamiliarity, social awkwardness, and in some cases arrogance and garrulousness. A tendency towards externalization, denial regarding separation, and alcoholism, along with stark dreams involving fragmentation of the body (p. 438).

It is difficult, perhaps impossible, to determine whether a particularly

intense dream can be viewed as a stressor or as a product of that stress, or both. Assessing the temporal order in which dreams change in relation to mood state may enhance our understanding of this relationship. For example, if dream changes precede mood changes, this may stem from a neurochemical change that will ultimately lead to the manifestation of a mood change. Also, if the change in dreaming can be isolated as a precise antecedent, just prior to the change, it may suggest that the dream itself plays a causal role in the mood change. Conversely, if the dreams merely reflect the change in mood, changes in dream content would occur after the shift and might then be considered an epiphenomenon (or a symptom) of that mood state. In this case, we might anticipate a difference in dream type between states, but those differences would follow rather than precede the mood change.

As noted, previous observations on bipolar dreams tend to be based on clinical observations of a single case study. Prior to our initial investigation, no known previous empirical study had assessed the relationship between the dreams of bipolar patients in relation to mood. It was, therefore, my belief that by the identification of a systematic relationship between these variables (REM sleep, dreaming and mood), we would be in a better position to explain the mysteries of dreaming and its functional relationship to mood.

In the preliminary study and follow-up study (Studies 1 and 2) we tested the assumption that qualitative changes in dreaming would be

evident in relation to mood state and mood changes in bipolar patients. A sample of dreams which vividly illustrates this contrast is appended.

2.12 PART TWO: HYPOTHESES

The specific hypotheses for each study are as follows:

Study 1:

As mentioned previously, the purpose of this study was to conduct a preliminary exploration into the nature of dreams in those with bipolar disorder for the purpose of illustrating a connection between dreaming and mood. Therefore, it was expected that:

(1) dream content would systematically reflect prevailing mood state, i.e., that a predominant theme would be representative of depressive, manic, mixed, and neutral mood states. Given the exploratory nature of this study, these themes were not specified at the outset.

(2) in the day or days just prior to a switch from one mood state to another, such as depression to mania or vice versa, dream content would undergo a thematic change. It was hypothesized that a specific (but unnamed) theme would mark this transitory period.

Study 2:

The goal of this study was to replicate the initial findings of the pilot project (study 1) and to extend these findings to include other pertinent factors, such as objective sleep measures. It was also of interest to use a comparative population of unipolar subjects (MDD) in addition to bipolar

subjects.

The specific hypotheses for this study were as follows:

(1) Bipolar subjects were expected to report significantly fewer dreams during depression than during hypomania.

(2) A change in dream content was expected to closely precede an upward shift in mood. Dreams of death would be more frequently reported on the morning of an upswing than in the immediate day(s) following and preceding this change.

(3) The content of the dreams reported by bipolars was expected to differ from that of unipolars. Bipolars were expected to report significantly more dreams of death.

(4) REM sleep latency would be state dependant in bipolar disorder and trait dependant in unipolar depressives. In other words, a significant difference in REM sleep latency between periods of depression and hypomania in bipolars was expected. Latency to first REM episode was expected to be positively correlated with mood, i.e., the lower the mood, the shorter the onset to REM sleep. In contrast, REM sleep latency was expected to remain more consistent in the unipolars, being pathologically shortened regardless of prevailing mood.

(5) On the night preceding a mood upswing in bipolars (the transition night), dreams with death themes would be associated with objective alterations in REM sleep. The specific nature of this alteration was unspecified.

Study 3:

This study was pragmatically engendered by the need for a means to promote upward mood swings using a swift and minimally intrusive method in order to achieve the goals of study 2. As phototherapy was chosen to achieve this, the opportunity to simultaneously tests for its effects was provided.

The specific hypotheses for this study were as follows:

(1) It was expected that the group receiving high intensities of daily light therapy would have a significantly larger improvement in mood that those receiving the lower intensities.

(2) It was expected that both males and females receiving phototherapy would improve similarly, but that bipolar patients might experience more notable mood improvements than unipolars because of their reputed sensitivity for light.

Study 4:

Beyond improving mood, light is said to inhibit melatonin secretion. As melatonin is directly implicated in sleep, one would naturally anticipate that mood improvements would be directly related to some measurable change in sleep. Although subjective improvements in mood are frequently reported following light treatments, a dearth of information demonstrating a corresponding change in sleep is reported. Moreover, as melatonin itself is a

soporific, one might anticipate that by suppressing it, there would be a notable detrimental, as opposed to beneficial, effect on sleep. I suspected that neither would be the case and that an alternate mechanism of action might account for bright light's effect on mood.

Study 5:

This was a natural experiment, and although not directly planned as a part of this series of studies, it was devised as an extension of the findings in the previous light studies. Artificial light was clearly found to be efficacious for mood in previous enquiries. At the same time, it was serendipitously noted that our current hospital architecture randomly affords a discrepant level of natural lighting to hospitalized patients; therefore, it was hypothesized that depressed patients in sunny hospital rooms would have a shorter length of stay than those in rooms without direct sunshine.

1. NOTE: Parts of the introductions presented in the studies that follow repeat certain topics that have previously been covered in this initial review chapter, including the aforementioned hypotheses. This has been done purposefully, so that: (1) the papers are presented in close approximation to their published form; and, (2) to prime the reader for the specific methodologies to follow.

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2.14 APPENDIX 1

A BIPOLAR PATIENT DREAMS IN DIFFERING MOOD STATES

DREAM 1: reported on the morning patient awoke in a hypomanic state.

I don't know how, but I died. I don't know why, but I had a feeling that it was in Australia. It was a very beautiful place, even the bloody...I don't like these places normally, but even the funeral home. It was all modern and everything and they hauled me in there and they took my blood and everything out and I knew about it, and I thought, "Gee whiz, what a place to die." Then they put me in a rose coffin and they waited until everybody came from the relatives. And all my relatives were happy and they said, "Gee whiz, X sure knows where to die." Nobody was sad, my mother wasn't sad...They liked me, but it was so strange that I knew everything, even though I was suppose to be dead. And I was in this bloody box and I seen them dig this hole and I seen them lower me down even though I was in the box and it was closed. And then when they put this dirt on top of me, it was like I was up...like I wasn't a body, I don't know what you call it...I was up on top, looking down and I seen them put these nice roses... flowers, they don't even have these flowers here. And it was so colourful, and the sky was beautiful weather, and everybody, and my mother was so happy.

And then my sister X, it was so strange because she said, " Gee whiz, I'd like to die here because this is so beautiful. So someone there in that country said. "well, we have this stuff that you can commit suicide and it doesn't even hurt." So she said, "maybe I'll do that so you won't be here alone," She said.. She went around and asked all the relatives and my mother what they thought. She said, "what do you think? I've been here quite a while..and they said, "well it's your business, it's a good place to die. So she said "I might do it." So she took this vile of stuff to die and then these same guys carted her into the same funeral home, which was a modern place and then someone, I don't know who, decided that they should have a double funeral, so they dug me back up. And they took me back to the funeral home, but they left me in the coffin. And then they got X ready, and I could tell everything that was going on, and I'm supposed to be dead. And while I was in there I started something inside the coffin. They were having visits for X. And my mother came over and she opened the door of my coffin and she said "Sunny [that's what she used to call me when I was a kid] Sunny, this is not the place to make noise!" Then she closed the door. She wasn't mad. Then they carted both of us out and another nice day, two holes out there and they planted us and they put this rich dirt on top of us and they put these beautiful flowers....

Again, I don't know where I was but I was up above there, just a few feet above. I don't think anyone seen me, I wasn't talking, I was just looking. But the feeling was no fear at all and I'm afraid of all that kind of stuff, but there was no fear. It was so colourful and I woke up then.

Subject's comment: It was so significant. I never had a dream like this. It was so colourful. It was like a holiday and nobody was sad. I thought it was proof that there is life after death and that I'm going to the right place or that I was going to win the lottery. I was so high when I woke up.

DREAM 2: Several days later in a depressed state:

It wasn't anything good... I dreamed I died again, but this time I really died. I don't know, somebody shot me or something ... and I just was just dreaming... I can't be specific, but everything was like that.
Subject's Comment: I don't feel so good, I'm just wiped out.

CHAPTER 3

3.0 STUDY 1: PREVAILING MOOD, MOOD CHANGES AND DREAMS IN BIPOLAR DISORDER [1]

3.1 INTRODUCTION

The analysis of dreams for diagnostic purposes has a long history, but little systematic study of dreams and their relation to specific illnesses has been done. Reviewing the literature discloses many fragments, anecdotes and opinions, but some of these are contradictory, and the totality is hard to summarize coherently.

Freud (1900;1991) proposed that psychopathology is often preceded by a disturbing dream. Clinical states are said to be reflected in a patient's dreams. Kramer et al. (1968;1991) suggest that improvement in depression may be heralded by changes in the patient's dreams. In a longitudinal nightmare study, Hartmann (1984) noted that subjects who became mentally distressed during the course of the study experienced frequent nightmares.

The relationship between state of health and dreaming does not appear to be limited to psychiatric conditions. Smith (1984) investigated the relationship between retrospective dream reports and physical outcomes with a large group of cardiovascular patients. Smith (1991) concluded that the severity of organismic dysfunction is indicated in the content of the patient's

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1 A version of this chapter is published as: Beauchemin, K.M., & Hays, P. (1995). Prevailing mood, mood changes, and dreams in bipolar disorder. Journal of Affective Disorders. 35, 41-49.

dreams. He found that dreams of separation and death were associated with a poor prognosis.

3.1.1 The content of normal dreams

Assessment of unusual dreaming is done in the light of our knowledge of ordinary dreaming. Hall & Van de Castle (1966) quantified home-recalled dreams of a large sample of college students in order to derive normative references for the manifest content of so called "normal" dreams. They found that even in what was taken to be a normal population, negative emotions within the dreams far outweighed the positive. Apprehension within dream content had the highest noted prevalence. Dreams of misfortune involving death were relatively rare with a frequency of less than 4 per 100 dream reports.

3.1.2 Mood and dreaming

As noted in the previous review chapter, most studies indicate that during depression dreams tend to be flat, prosaic, short, and less memorable (Riemann et al., 1990; Van de Castle & Holloway, 1970). Other studies have found that depressives' dreams involve thwarting or victimization (masochistic dreams) (Beck & Hurvich, 1959; Beck & Ward, 1961). Whitman et al., (1970) collected over 90 dreams of depressed subjects and reported that 33% of these reflected themes of helplessness and hopelessness compared to

only 8% of controls. More recently, Cartwright (1992) found that depressed women reported frequent "masochistic" dreams following a divorce. Riemann et al. (1990) reported that in a sample of inpatient laboratory dreams collected, depressed subjects did not reveal a high level of "masochistic" dreams. Rather, they found a very low level of overall scorable dreams, most of which they described as rather mundane.

Reports of less dream activity, or more mundane dreams during depression does not necessarily reflect a corresponding change in REM sleep architecture. There is no evidence to suggest that the overall percentage of REM sleep declines in depression. One explanation for the blandness of depressive dreams may be connected to phasic REM changes. Oswald et al.,(1963) monitored the eye movements of depressed patients and noted that although the overall time spent in REM was normal, the frequency and intensity of these movements were diminished in depressed subjects. However, there is much evidence suggesting the contrary; namely, that there is an increase in REM density associated with depression along with the well documented finding of a reduction in latency to the first REM period (Kupfer, 1984). Nevertheless, although there is a strong correlation between REM sleep and dreaming, dreaming can also occur in non-REM (NREM) sleep (Foulkes, 1996), and therefore, dream reports alone are not reliable indicators of underlying sleep physiology.

Kramer et al. (1976) write that dream content reflects a continuity of

waking thought. "It is [also] possible that the 'barren' dream narratives reported during depression may be a function of reporting style, that is itself influenced by the depression (Kramer, 1970; p.150)". Whitman et al., (1970) tested this assumption and found that depressed subjects showed diminished ability to report fantasy.

It should be noted that most of the aforementioned studies profess to focus mainly on the dreams of what were called primary endogenous or unipolar depressives. However, the diagnostic categories studied are not always clear, whether because of the authors' incomplete accounts, the different criteria used in the past, or the provisional state of nosology in psychiatry; but probably most early studies were done mainly on unipolar depressions, as distinct from the depressed phase of bipolar disorder. Whether such dreams are also representative of the depressed stage of bipolar disorder is unknown.

3.1.3 Bipolar dreams

If a clear relationship exists between mood and dream content, qualitative changes in dreaming in relation to mood state should be evident in the dreams of bipolar subjects, since the hallmark of bipolar disorder is fluctuation in mood states.

Hartmann (1968; 1989) writes that the shift from depression to mania commonly occurs in sleep and the patient awakens manic. He speculates that

a dream might in some way be causal to the mood shift. Levitan (1977) hypothesizes that the onset of mania is directly related to the memory of a painful experience which is relived in a dream, and has noted many instances of peculiar dreams involving trauma and bodily harm preceding shifts to mania. Stone (1978) notes that several subtle changes can alert a clinician to an oncoming state of mania, one of which involves dreams of bodily fragmentation.

As noted, observations on bipolar dreams tend to be anecdotal, involving single case studies. No previous empirical study has described the dreams of bipolar patients by systematically relating dream content to prevailing mood and mood changes. Thus, in this preliminary exploratory study we sought to address the following questions:

(1) Are there differences in dream content within the various mood states of bipolar disorder (depressed, neutral, mixed and manic)?

(2) Do dreams during the depressed phase of bipolar disorder resemble those reported in the literature as representative of unipolar depressives?

(3) Are there changes in the manifest dream content <u>preceding</u> mood changes such that these dreams may in some way be linked to the shift or serve as a marker of these shifts?

These goals required the use of an appropriate dream classification scale for content analysis. We found no suitable scale in existence, so that an incidental product of this study was an approximation to the scale which will ultimately be appropriate for the classification of dream content in bipolar affective disorder.

3.2 METHOD

3.2.1 Subjects:

Six unpaid subjects were recruited in the psychiatric outpatient clinic at the University of Alberta Hospital. There were 2 females and 4 males, ranging between 33-59 years of age (mean=45.2). Inclusion criteria: Bipolar I as defined in DSM IV (American Psychiatric Association, 1994); exclusion criteria: absence of first degree relatives with a major affective disorder. Treatment was not affected by the investigation, so that subjects continued to take their regularly prescribed medication throughout the study. Medication profiles varied between subjects and consisted of various combinations of antidepressants, anti-manic drugs, and lithium.

3.2.2 Procedures:

Initial contact with subjects was made during a controlled remission of their illness, and informed consent was obtained. Then the first author (KB) telephoned each participant 3 times per week, in order to solicit reports of dreams recalled from the preceding night and a mood rating for that particular morning. Regular calls were placed on Tuesdays, Thursdays, and Saturdays between 5:30 am and 9 am (at each subject's requested wake-up time). All telephone calls were audio-taped using a Sony recorder with a telephone tape adapter, to facilitate accurate transcription of the dreams with minimal intrusion. This procedure continued for a period of 6 months,

unaltered unless the subject became hospitalized. If a subject became hospitalized, participation resumed upon release.

A subjective rating of prevailing mood was rated by each participant by using a numerical mood scale supplied at the outset. This scale was a numerically incremental rating, ranging from 0, for severely depressed, to 10, for extremely manic, and included a non-numerical, categorical rating for mixed mood states. Each subject was also assigned a corresponding mood rating by KB based primarily on clinical observations. To the best of her ability, she made this rating without reference to the dream content reported. Her rating was guided by such things as tone and speed of speech and both overt and subtle indicators of reference to state, paying particular attention to the symptom criteria for mania and depression listed in the DSM-IV, for example, evidence of inflated self-esteem and risk-taking behaviour in the case of mania. Overall, patient status was also monitored by regular consultation with the attending physician, (PH, in 5 of 6 cases) who assessed patients approximately every 5 weeks at their regular outpatient appointment. After the 6 month collection period, all dream reports were transcribed verbatim, one dream to a page.

A global rating of corresponding mood was then assigned by averaging the subject's rating and the researcher's rating for each day. The exception to this was the case of a mixed state which could not be averaged and was therefore assigned a mixed rating if defined as such by either raters (subject

or KB). These final mood ratings from 0-10 were then divided into four categories: 0-4 represented depressed, 5 neutral, 6-10 manic, and M, mixed states.

3.2.3 Analysis:

All the dream reports were identified solely by coded numbers and then placed in random order. Each investigator individually classified the dreams produced. PH was able to do so partially "blind", except that a few dreams enabled him to identify the patient because of some familiar reference. He was, however, always blind to the patient's mood at the time of each dream. After reading all the dreams several times in different sequences, PH made notes of what seemed to be outstanding or dominating types of dreams or themes, and produced Scale PH. This categorisation was approximately congruous with that produced independently by KB (see Appendix 1).

Both scales were then used in the analysis in case one was more illuminating than the other. Each researcher first scored the dreams independently. Then these results were compared and resulted in a high level of inter-rater agreement (Spearman r =.92). The few discrepancies that did occur between raters were then discussed and resolved by consensus. As many categories as were applicable to elements contained within each dream were assigned; categories were not mutually exclusive and some dreams

contained elements of several scales.

Freidman's non-parametric analysis of variance, on Kwikstat statistical program for IBM (Texasoft, 1984,1993) was used to determine differences in dream themes within each of 4 mood states: depressed, neutral, mixed, and manic. We then compared the dream themes reported just prior to a mood shift with the dream themes reported in neutral states, in order to determine whether a dream content marker or predictor was associated with an impending mood shift.

We made three comparisons:

(1) dreams reported on the day of a significant mood shift (defined as a change of 2 or more points in either direction on the mood scale, excluding shift to neutral and mixed states) versus the dreams reported in all neutral mood states;

(2) dreams reported for the week prior, up to and including the day of the mood shift, versus all neutral states;

(3) The data for the week prior to the shift, but excluding the actual day versus all neutral states.

3.3 PRELIMINARY RESULTS:

Of 429 inquiries made, a total of 335 dreams were reported. This was a rate of 0.78 dream reports per inquiry, averaging 2.33 dreams per person per week. Of these dreams, 142 featured unsuccessful occurrences, 116 were mundane, 61 involved death or bodily harm, and 44 were bizarre.

Dream themes in association with concurrent mood state (depressed, neutral, mixed, manic)

A one-way non-parametric analysis of variance with 4 groups, each representative of a given mood state was used. Two significant patterns emerged regarding neutral and manic states, while no clear association could be found with either depressed or mixed states. Scale PH-3 (occupational-neutral or successful) was found to be associated with neutral states ($Q=9.21, df=3; p<.03$). Scale KB-3 (mundane) was also associated with neutral states ($Q=7, df=3; p<.07$). Both of these scales represent a type of mundane, uneventful, routine or occupational dream theme.

In manic states, scale KB-1 (bizarre) was associated with elevated moods ($Q=7.87, df=3; p<.05$), while PH-1 (bizarre) approached significance ($Q=7.44, df=3; p<.06$). These scales both encompass improbable and grotesque themes. A detailed definition of these scales is listed in appendix 1.

Predictive models - dreams associated with mood shifts

1. Dream themes reported on the day of a mood shift versus all dreams reported in neutral states.

Scale KB-2 (death & injury) dreams were frequently reported on the morning of the day of a mood shift ($Q=5.00;df=1,p<.03$). Also scale PH-2c, (violence and injury - unsuccessful), approached significance in association with the morning of a mood shift ($p<.08$). Conversely, scales PH-3, PH-4 and PH-5 (routine occupational- all types) were rarely reported on the morning of the day of a mood shift.

2. Dream themes reported the week prior to mood shift (excluding the actual day of the shift) versus dreams reported in neutral states.

No significant differences on any dream scales were associated with the week prior to the mood shifts when the data from the actual morning of the transformation were removed.

3. Dream themes reported during the week prior to a mood shift (including the actual day of the shift) versus dreams reported in neutral states.

When the data were combined for the week prior to the shift including the day of the shift, Scale KB-2 (death and injury) dreams continued to show a statistically significant association with upward mood shifts ($Q=4.00;df=1,p<.05$). Scale PH-2c (violence and injury - unsuccessful) again

approached significance ($p<.08$).

We then split the data on the day of these mood shifts between shifts to depression and shifts to mania and compared the two in terms of the prevalence of dream elements. Only the data for 4 subjects could be used in the analysis as 2 lacked shifts to both states that could be compared, which limited our ability to discriminate.

Shifts to mania contributed more than did shifts to depression to the emergence of significant dream themes. Many shifts to depression actually lacked a dream report. Although dreams of death may sometimes precede shifts to depression, it was the absence of a dream report which was more clearly associated with an oncoming depression. A sample of dreams reported in various mood states is detailed in appendix 3.

3.4 DISCUSSION:

Dreams reported by our bipolar patients appear to differ in content from normative data provided by Hall & Van de Castle (1966). Many of the dreams reported by our patients reflected failure, as opposed to apprehension or were instead mundane and lacking in emotional overtones. We also note a very high occurrence of death-related themes in our patients' dreams. The frequency of these dreams was .18 (61 of 334), five times greater that the frequency reported in the Hall & Van de Castle norms. This preoccupation with death related themes may be related to the underlying psychopathology and may reflect an unstable condition, such as was found by Smith (1984;1991) in the dreams of his cardiovascular patient group.

Our preliminary results indicate that dream content differences do exist within mood states. Neutral mood states appear to be associated with mundane, routine and occupational themes. Conversely, elevated mood states appear to be associated with bizarre and improbable themes. Dreams during the depressed phase of bipolar disorder do not seem to resemble those reported in the literature of patients with unipolar depression, at least in terms of "masochism"; although there was some evidence to suggest that dreams in depressed states were shorter and more barren. The lack of "masochistic" dreams in association with depression might be a reflection of a difference between bipolar depression and unipolar ("endogenous") depression.

Themes related to death, injury and mutilation were present in dreams immediately preceding mood shifts. These dreams were associated with both the onset of mania and depression, but more prominently associated with an upward shift, supporting suggestions by Levitan (1977) and others. A diagram (see figure 1) illustrates the way in which dreams of death precede a shift to mania.

Awakening in a hypomanic state after a specific type of dream calls to mind Hartmann's (1968) suggestion that the dream might in someway be causal to the mood shift; but whether the dream has a causal role or is merely an epiphenomenon remains speculative. These dreams might instead be directly reflective of neurophysiological changes that cause or accompany mood changes. This idea echoes Hobson's (1988) Activation-Synthesis hypothesis of dreaming which states that physiological changes (activation) occur neuronally, then a dream is synthesized "which denotes the best possible fit of intrinsically inchoate data produced by the auto-activated brain-mind (p. 204)."

Given that switches towards mania frequently occur in sleep, and that one is more likely to recall the most recent dream experienced, it is not surprising to find altered dream content on the first day of an upward mood shift. However, the finding that dreams heralding mood changes had death related themes, and were different from the bizarre kind of dream which marked continuing elevated moods was intriguing. Dreams preceding

upswings in mood were marked not so much by their quality, as by a particular content: death, dying and bodily injury. In light of the specificity of this repetitive theme, it is difficult to subscribe to the idea that dreams are randomly contrived epiphenomena synthesised to accompany the antecedent physiology: turbulent bizarre dreams may reflect the underlying physiology of hypomania, but the theme of death (arising as it did in dreams which ranged from tranquil to violent) is harder to explain in this way.

It is also unlikely that the dreams at the transition point to mania are a mere reflection of physiological changes that have already taken place (but not yet detectible by mood measures), again because the dreams that occur within the state of mania, as opposed to those that foreshadow it, differ in their characteristics. The specific theme of death implies that there may be a psychological rather than, or in addition to, a biochemical link in the relationship between mood and dreaming.

We note again that although death related dreams were significantly more prominent only on the night preceding a mood shift, the trend appeared to start some time prior to the actual shift (see figure 1). This could not be demonstrated statistically because the period preceding the shift, in which these dreams occurred, may have encompassed any mood state, and therefore lacked a discrete comparative reference.

Some methodological limitations merit a brief word. The patient sample seems small; but cooperative and persevering bipolar patients with

frequent mood changes are uncommon. Also, a larger number of patients would have called for an extra observer, because of the time consuming nature of the investigation. Having the mood and the dreams recorded by separate observers, clearly desirable, would also have required an extra investigator and would have made the interviewing process more tedious for the patients; correspondingly, the remarkable compliance and cooperativeness of our subjects might have been eroded by multiple applications of affective rating scales. Our dream scales, of which a more detailed account is offered shortly, would best have been devised by workers who had not recorded the dreams and did not know the patients, but again this would have called for extra personnel. All the limitations mentioned in this paragraph are connected to the preliminary nature of our study. Those who have made similar forays will appreciate this more readily than readers accustomed to areas where the constructs are mature. At a practical level, our finding of death related themes as patients swung into elevated moods was counterintuitive and makes lack of blindness as a methodological flaw less weighty; money is not available for large research teams when there can be no assurance of positive results; and ethically, patients cannot be put to too much trouble in speculative causes.

Our dream scales call for a longer review. At present, an investigator who is assessing anxiety or dementia or other common conditions has at his or her disposal a series of measurement tools which have been validated and

about which much is known. Readers of research papers justifiably expect that results will be reported in terms of these well known rating scales. Of course, at one time there were no such scales, and they had to be invented and refined.

Classification methods devised for the dreams of normal subjects would probably not be applicable to the dreams of clinical patients, such as bipolar patients for whom abnormal sleep and highly unusual dreams are the rule (and, as is the case here, the main topic of the inquiry). It follows that willy nilly we have to settle upon some way of sorting the dreams we have recorded into natural categories.

There is no royal road to classification. The most promising approach to settling on such a classification is the Baconian one of using an intelligent and educated observer who is familiar with many of the pitfalls of classification; the researcher must learn as much as is possible about the things which he or she hopes to classify; then after some rumination, a tentative classification will arise. This classification system will reflect cultural and personal psychological aspects of the researcher, and will not arise solely from spontaneous clustering of the data. It will also be influenced by a priori expectations including those engendered by other work e.g. the previous developed masochistic scales (Beck et al., 1959; 1961). Involving two independent classifiers reduces these influences. It may be regrettable, but it is inevitable, that mature scales are not available for early studies such

as ours.

Based on the apparent usefulness of our classification schema, we offer a revised scale for use and refinement in further inquiries into the dreams of bipolar subjects (see appendix 3). Despite inevitable constraints, and the preliminary nature of this undertaking, our results suggest that prevailing mood, mood changes, and dreams are related in an intricate and unexpected way.

At the time that this paper first appeared in print, my associate and I were in the late planning stage of a more extensive investigation into bipolar patients' dreams, incorporating neurophysiological as well as anamnestic data. This results of this now completed study are reported in the subsequent chapter.

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3.6 Appendix 1: MOOD RATING SCALE

Please choose one of the following numbers to rate your current mood state:

I am feeling:

10= severely manic

9 = extremely high, exhilarated or agitated

8 = very high and exhilarated

7 = somewhat high

6 = just slightly up

5 = neutral ... neither up nor down

4 = just slightly down

3 = somewhat depressed

2 = very depressed

1 = extremely depressed

0 = severely depressed

M = mixed mood

(both somewhat depressed & somewhat high)

*** the researcher also used the same scale to rate each subject's apparent mood. In this case "I am feeling" is replaced by: "on the basis of my clinical observations, the subject appears to be feeling: "**

3.7 Appendix 2: DREAM CONTENT RATING SCALES

SCALE 1: PH

1. Bizarre, grotesque, disgusting
2a. Violence and Injury: successful or neutral dreams of action (killing, shooting, beating up, etc.)
2b. Nonviolent death; dying; funerals
2c. Violence and Injury: unsuccessful
3. Standard routine occupational or hobby or holiday activities. successful or neutral
4. Standard routine - unsuccessful
5. Standard routine - exalted
6. Food and Eating

SCALE 2: KB

1. **Bizarre themes**.- this category includes dreams of very unusual or improbable events, such as those containing magic, delusions, aliens, flying, unusual creatures, and experiences out of the ordinary.
2. **Death & Injury**: - dream contains elements of death, or threat of death to self or others. This category also includes themes of combat, mutilation, or serious bodily injury and elements related to death (funerals, coffins, corpses, the deceased etc.)
3. **Mundane themes**. -contains no affect, low activity, deals with ordinary daily topics and people, and does not contain any of the qualities of KB 1,2 & 4.
4*. **Masochistic - Unsuccessful occurrences**. Dreamer experiences thwarting, criticism, failure, loss, abandonment, inability to achieve goals, victimization, punishment, etc.

* based on a modification of the Beck et al., 1959;1961 Masochism Scale

3.8 Appendix 3

SAMPLE OF REPORTED DREAMS

Dreams of death the night preceding shift to mania:

(1) *I was dreaming about dying ... how to get the inner death ring back into yourself. [I] was going through the graveyard and seeing people who are dead come back to life, like a horror show. It was gross.*

Bizarre dream in hypomanic state:

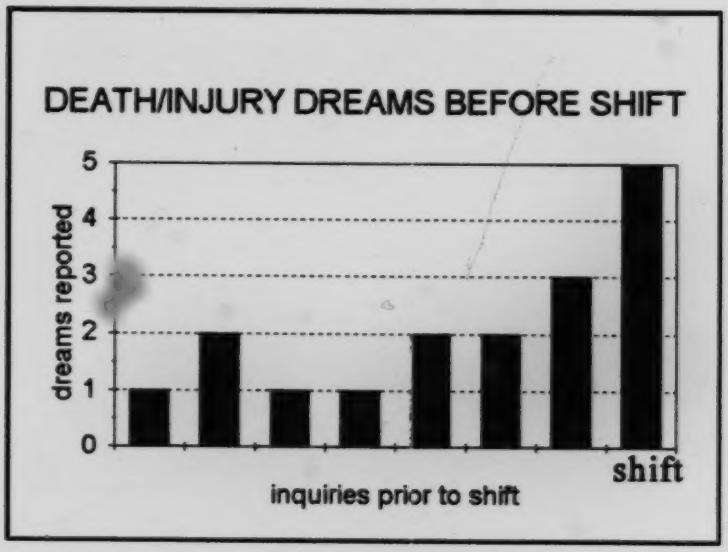
(2) *I dreamt about some alien space people. They weren't in a spaceship, they kind of just floated down and there was quite a few of them and there was kind of like an army of space aliens.*

Routine, occupational dream in neutral mood state:

(3) *I was travelling with my wife. We were at a hotel and we were getting ready for the evening and it was a very nice hotel, nice room, everything was nice. It was a business trip.*

3.9 Figure 1

DEATH DREAMS PRECEDING MOOD SHIFTS UPWARD



*** based on thrice-weekly reporting of all patients (N=6)**

*** Usual rate of these dreams in all instances was 0.18 (61 of 335 dreams)**

CHAPTER 4

4.0 STUDY 2: DREAMING AWAY DEPRESSION: THE ROLE OF REM SLEEP AND DREAMING IN AFFECTIVE DISORDERS [2]

4.1 INTRODUCTION

Despite prodigious artistic, philosophical, and scientific preoccupation, the function of REM sleep and dreaming remains unknown. A large number of psychiatric research reports has shown that both REM sleep and dream content are profoundly altered in affective disorders. A precise analysis of the relationship between mood, REM sleep and dreaming may, therefore, enhance our understanding of both REM sleep and affective disorders. This study reflects this goal.

This necessitates a review of the literature which, though we aim to be brief, has to range fairly widely. We shall first consider the work done on sleep and affective disorder then more specifically on dreams and affective disorders.

4.2 SLEEP AND AFFECTIVE DISORDERS

4.2.1 Sleep and unipolar depression:

Several anomalous characteristics of sleep are reported in association with "endogenous" depression. These include an abnormal temporal

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2 A version of this chapter is published as: Beauchemin, K.M., & Hays, P. (1996). Dreaming away depression: The role of REM sleep and dreaming in affective disorders. Journal of Affective Disorders. 41, 125-133.

distribution of REM sleep (Vogel et al, 1980), with an overproduction of REM in the first third of the sleep cycle, both in quantity and intensity (Van den Hoofdakker et al., 1986). The most consistent finding reported is that depressives have a reduced REM latency - a decrease in the usual 90 minute non-REM sleep episode that precedes the first REM episode of the night. This reduced REM sleep latency is so pervasive that it has been proposed as a biological marker of depression. There is also a suggestion that this may be a "trait-like" marker because in many instances this abnormality persists in remission (Kupfer, 1984). Also, first degree relatives of depressive patients are frequently concordant for REM latency, though they have not had a depressive episode (Giles et al., 1987). "A reduced REM latency in the family members of reduced REM latency probands showed a concordance rate of 70.6% regardless of psychiatric history, and the relative risk for unipolar depression among relatives with reduced REM latency was almost three times greater than for relatives with normal REM latencies" (Fleming, 1994; p.339).

4.2.2 Sleep and bipolar disorder:

Reports of the sleep of depressed patients are abundant, whereas sleep studies confined to bipolar patients are both scarce and inconsistent in their findings. Several attempts have been made to document sleep during particular phases of bipolar disorder. For example, Hudson et al., (1988)

report that manics exhibit decreased total sleep, decreased REM latency, and increased REM activity; while Hartmann (1968a) reports that REM latency increases in mania. Linkowski and others (1986) found that although total sleep time was reduced in mania, there were no significant differences in REM sleep, or any other sleep stages, when compared to matched controls. In an EEG study of bipolar patients during a depressed phase, Thase et al., (1989), found no significant reduction in REM latency, but did report a decrease in stage 1 sleep and a slight increase in total REM percent. REM latency in bipolar disorder has interesting variations, but is not consistently reduced, and it might be that it is state dependant rather than trait dependant. We return to this point later.

These studies describe sleep during depression or during mania, but not the ongoing changes in sleep in particular subjects that accompany the transition from one mood state to another. Generally, comparisons are made to various types of control groups, but because sleep patterns vary (Carskadon & Dement, 1994) it is preferable to make an accompanying comparison of subjects' sleep in one state with their sleep in another.

If shifts in mood actually occur in sleep, as suggested by Hartmann (1968b) an intriguing possibility exists that one might obtain records of sleep during nights when the mood is in a state of actual transition. However, the requisite serial polysomnography over a long period would be expensive and intrusive and, addressing one of our areas of interest, would probably modify

the subjects' dreams.

These problems are surmountable with a recently developed technique for ambulatory sleep monitoring, the Nightcap, developed by the Harvard sleep research group (for a review see Olusola et al., 1995).

With the use of a Nightcap, it becomes feasible to capture the sleep parameters that accompany actual and ongoing mood shifts (i.e., shift to mania and depression) while assessing sleep quality and dream characteristics associated with these states.

4.2.3 Dreams and affective disorders

Breger (1967) speculated that REM sleep dreaming functions as a means to integrate recent emotionally charged experiences with pre-existing similar and successful memory schemata. Several researchers have since proposed the possibility of a mood regulatory function for dreaming (Kramer, 1993; Perlis & Nielsen, 1993). Kramer (1993) has shown that there is an decrease in "unhappy" and "anxiety" subscales in mood measures from pre to post sleep in normal subjects. Cartwright & Lloyd (1994) report that depressed subjects exhibiting a shorter REM latency following a life stressor have increased accompanying reports of early night dream intensity. They interpret this finding as support for the hypothesis that reduced REM latency (which is accompanied by earlier dream intensity) "may represent a compensatory mechanism when negative affect exceeds normal limits" (p.

250).

As discussed at length in previous chapters, there appears to be an intricate relationship between sleep, dreaming, and mood state in bipolar illness. The mechanism and the essentials of the trigger of mood swings in bipolar disorder are unknown. Reviews of the topic support clinical impressions, that stressful occurrences frequently precipitate a shift (Goodwin & Redfield Jamison, 1990). Severe stressors have a known effect on dream content as shown in post-traumatic-stress disorder. Moreover, some types of dreams might themselves be viewed as stressful, so that: "traumatic events in dreams [may] themselves [be] a source of stress which contributes to the production of physiological misfunction (Levitan, 1982)." Therefore, stress might precipitate changes in dream content so that the dreams themselves precipitate mood changes.

In the preliminary study (Study 1), we looked at the relationship between dream content, mood state, and mood changes in bipolar disorder, and found a relationship between prevailing mood state and dream content. Unexpectedly, it seemed that dreams containing death themes were either harbingers or markers of upward mood shifts. In the present study, we sought to replicate this finding and to further explore whether sleep physiology reflected any aspect of the mood changes.

At the time we initiated this study, we were conducting an efficacy trial for bright-light therapy as an adjunct treatment for non-seasonal

hospitalized depressed patients (unipolars & bipolars). In contrast to drug therapies, light therapy tends to promote an improvement in mood within 3 to 5 days (Lam, Kripke and Gillin, 1989). There is also some evidence for increased light sensitivity in bipolars (Lewy et al., 1985), and a suggestion that light can actually induce hypomania (Pande, 1985). We saw an opportunity to exploit this for the purposes of the present study.

4.3 HYPOTHESES:

Dreaming:

In accordance with the findings of our pilot study, we expected that:

(1) Bipolar subjects would report significantly fewer dreams during depression than during hypomania.

(2) A change in dream content was expected to closely precede an upward shift in mood. Specifically, we anticipated that dreams of death would be more frequently reported on the morning of an upswing than in the periods following and preceding this change.

(3) Dreams reported by bipolar patients were expected to differ in content from those of unipolar patients; that is, bipolar patients were expected to report significantly more death dreams.

Sleep:

(4) We tentatively hypothesized on the basis of our literature review that REM sleep latency is state dependant in bipolar disorder and trait dependant in unipolar depression. Therefore, we anticipated a significant difference in REM latency between periods of depression and hypomania in bipolar patients. Latency to first REM period was expected to be positively correlated with mood, i.e., the lower the mood, the shorter the onset to REM. REM latency was expected to remain more consistent in the unipolars, being pathologically shortened regardless of prevailing mood.

(5) We expected that on the night preceding an upswing in bipolars, dreams with death themes would be associated with objective alterations in REM sleep.

4.4 METHOD

4.4.1 Subjects:

We recruited patients over six months in the University of Alberta Hospital psychiatric wards. All inpatients hospitalized for a major depressive episode (whether previously diagnosed as unipolar or bipolar) were invited to take part in the trial, unless: (1) their attending physician did not agree to their participation, (2) the patient was receiving, or scheduled for ECT (electro-convulsive-therapy), or (3) an anticipated release from the hospital would have left too little time for participation in this trial. Qualifying subjects were then given an information sheet and asked to sign a standard consent form in accordance with the ethical requirements of this institution. We diagnosed these patients as bipolar or unipolar: bipolar subjects met the DSM-IV criteria for bipolar disorder (American Psychiatric Association, 1994), and were, at the time of recruitment, in a depressed phase. Non-bipolar or unipolar patient had the diagnosis of a major depressive disorder. As far as the state of psychiatric nosology allows, we recruited homogenous categories (unipolar & bipolar). In all, 24 subjects participated, 12 unipolar, and 12 bipolar. Sixteen were female, 8 male; the average age was 35 (range, 21-63).

All subjects continued to take prescribed medications throughout the study, mostly SSRI antidepressants (N=21) with the exception of a small number of patients (N=3) on adjuvant lithium or lithium alone. As most

measures were taken within-subjects, (i.e., mood measures, sleep physiology) the effects of drugs on sleep and dream content was expected to remain approximately stable within each subject. In most cases the drugs had been started some time before the trial.

4.4.2 Procedures:

Following initial recruitment, KB visited each participant on the wards every morning except Sundays for 7 to 10 days. During these visits, subjects had their mood assessed; reported all dreams recalled from the preceding night; and received 30 minutes of light-therapy (in the case of those simultaneously participating in the light study).

Whenever possible, each patient was also instructed to wear the Nightcap to sleep on the first, third or fourth, and last day of the trial. On scheduled Nightcap evenings, the researcher (or a designated staff nurse) again visited prior to bedtime (usually between 9-11 pm) to assist and instruct the patient in its use.

Mood was assessed daily by a rating scale devised in our pilot study which consisted of an ordinal scale from 0, severely depressed, to 10, severely manic. Mood was also assessed intermittently with the Profile of Mood States (POMS-Bipolar form) (McNair et al., 1988). We attempted to have each subject wear the Nightcap overnight on days 1, days 4, and days 7, and to complete the POMS upon awakening, while recognising that in the

turbulent setting of an inpatient psychiatric unit, with sick and sometimes suicidal or suspicious patients, recordings would frequently be incomplete. The protocol continued each morning for 7 to 10 days with each patient, in conjunction with the light-therapy trial, or less in the case of an individual patient being unexpectedly released. The "no light" group underwent the same protocol with the exception of the light-therapy. Due to the limited number of available subjects, equipment, and manpower, only 1 or 2 subjects participated at any given time so that recruitment spanned a 6 month time period.

4.4.3 Analyses & Instruments:

SLEEP: The Nightcap was used to record several nights of sleep with each patient. The Nightcap is a reliable and compact bedside computerized unit that records eyelid and body movements and based on an algorithmic ratio of these two measures can determine sleep latency and REM and non-REM sleep stages, for up to 30 nights (Stickgold et al., 1994). The nightcap itself merely stores raw data, which must then be down-loaded to a PC for analyses. This was done on a Macintosh computer, using software developed and kindly provided by the Harvard Laboratory of Neurophysiology (Stickgold, 1995; The NC Analyzer). This program provides an interpretation of measures of interest and plots a sleep histogram of the night.

The Nightcap offers minimal intrusion, low cost, and facilitates ongoing monitoring of unattended sleep. In a study of the Nightcap's reliability, analyses suggest that this apparatus is sufficiently sensitive to discriminate between REM and NREM sleep and the algorithm software program is in agreement with 85.6% of EEG-determined sleep states on a minute-by-minute basis. This was calculated in trials in which both the EEG and the nightcap are worn simultaneously. Sleep onset and REM onset were both predicted within 1 minute of EEG determined onset (Mamelak & Hobson, 1989).

DREAMS: All dream reports were transcribed verbatim. Following transcription, patient identification was temporarily removed and these dreams were then randomly sorted and then scored for content using our Revised Dream Content Rating Scales (see appendix 1). In addition, we also employed the Gottschalk & Gleser Anxiety Scale (Gleser & Gottschalk & Springer, 1961) for a measure of dream anxiety. This classification and rating was completed separately by both the researchers and again by an independent rater.

MOOD: The patient's daily rating of his or her mood was a subjective rating on a numerical scale provided. A corresponding researcher's rating was also made daily for each patient using the same scale. This was made on the

basis of general clinical observation. In most cases, as noted in our previous use of this scale, the 2 ratings (patient's & researcher's) were very close, except in cases where the patient lacked insight into the prevailing abnormal mood. These two ratings were averaged for one daily global rating score which was then used in the statistical analyses.

Besides this subjective mood measure, the POMS-Bipolar Form was used intermittently, in most cases, every second or third day. We added up the raw POMS sub-scale scores to achieve one representative global mood score.

LIGHT: We used standard artificial light boxes (SUN-RAY) at 10,000 lux in 10 patients, 2,500 lux in another 10 patients and no light in 4 patients. This systematic variation was necessitated by their concurrent participation in a simultaneous study on the efficacy of light therapy.

4.5 RESULTS

Our first undertaking was to establish the reliability of our measures. We preferred to use our own mood measurement scale because this was recorded daily while the POMS measures had been intermittent. Reliability was measured as a correlation and was r=.86 between mood scales recorded on concurrent days. This validated and justified the use of our scale for the subsequent analysis.

Next, we attempted to determine the possible confounding effect of light-therapy on sleep. We had hoped that it would at once improve the mood and at the same time not alter sleep patterns radically. A multivariate analysis of variance indicated that light group assignment (high light, low-light, and no light) had no apparent effect on REM sleep latency, REM percent, or REM density.

Despite the turbulent nature of patients one might expect with variable and psychotic mental states, these patients were in most cases persevering and cooperative so that in addition to daily mood and dream reports, in most cases at least 2 nights of sleep and 2 POMS were recorded for each participant.

In total, we collected 80 dream reports with corresponding mood ratings. In the few instances where a subject reported more than one dream from the same night, these reports were combined, making 74 dream reports. The two authors scored each dream report independently, PH being blind to

the patients' identities and diagnoses, and then met to compare scoring results. Most scores were identical and those few that differed were recoded by means of consensus. Next, we hired an independent rater to score the dreams. This third rater was blind to the study's hypotheses and naive to this area of research. She independently scored all 74 dreams on both our scale and on the Gleser & Gottschalk Anxiety Scale. These ratings were largely in agreement with our ratings (91% and 88% respectively). For the sake of objectivity and simplicity, we then analyzed all data solely in terms of this unbiased rater's scoring.

DATA ANALYSES:

It was necessary to use several methods because of the breadth of our hypotheses:

1) SLEEP: A general correlation matrix was first computed between all variables measured, of which 3 measures were found to be significantly correlated at $p<.05$: POMS total raw score and our global mood rating ($r=.65$) ; POMS and REM latency ($r=.67$); and REM sleep percent and REM sleep latency (inversely correlated $r= -.44$). Next, a linear regression model was used to test the assumption that REM latency, REM percent, eye-movement density and dream anxiety levels predicted morning mood. Each of these predictors was tested and subsequently removed if not significant. This resulted in a model in which REM latency and dream anxiety

significantly predicted morning mood ($F=3.55$, $df=2,26$; $p<.05$). Although REM latency by itself only approached significance as a predictor of mood, it became apparent upon closer scrutiny of the raw data that the linear trend was actually weakened by inclusion of the unipolar subjects. Therefore, a subsequent t-test for paired samples was computed to compare REM latency in low versus improved mood states within subjects for each group (unipolar patients and bipolar patients). We found that there was no significant difference in REM latency between low and improved mood states in unipolars, although it actually approached statistical significance, but in an unexpected manner. That is, as unipolar patients' mood improved, their REM latencies tended to **decrease**. This was reversed for the bipolar patients, whose REM latency **increased** with a corresponding mood improvement. The mean REM latencies were as follows: in unipolars, 69 minutes depressed to 39.5 minutes with improved mood; bipolar mean REM latencies were 40.6 increasing to 90.1 with mood improvement. However, only 8 bipolars and 4 unipolars could be used in this analysis as not all patients exhibited both mood states or had sleep recordings reflecting these.

Seven of the nights recorded actually coincided with an upward mood shift in bipolar patients: all had dreams of death that night, and 3 awoke directly from REM and from that dream; of these last 3, 2 were hypomanic on awakening.

2) DREAMS: We first attempted to compare the general content of dreams

reported in bipolar patients versus unipolar patients to see if they were uniquely different in content. We found that the unipolar patients reported significantly fewer dreams overall and, of those reported, mundane themes (sub-scale A) were most frequent. Bipolars reported more dreams and these dreams contained more violence (sub-scale D) and more death (sub-scale E)(chi-square = 29.1, df=5, p<.0005).

We subsequently sorted these dreams according to prevailing mood states: depressed and not depressed. Here we again found that when depressed, unipolar subjects reported fewer dreams and of those reported, content was still mundane (sub-scale A), and more unsuccessful (sub-scale B) in nature (chi-square = 9.69, df=4; p<.025). There was not enough data to determine any change in this content when mood improved. Also among unipolars one category contained no observations (bizarre, sub-scale C) which necessitated its being dropped; however, the lack of bizarrerie in the dreams of unipolars is an interesting finding. In the bipolar group, depressed patients showed roughly equal representations across all dream categories, but as mood improved they reported more death dreams (sub-scale E). (chi-square = 15.4, df=5; p<.005). A detailed description of the scale used is provided in appendix 2.

Next we looked to see if death dreams were indeed significantly associated with a mood change upward. This was again the case for bipolars. Of the 21 death dreams reported in total, 18 were from bipolars; all these 18

were reported within a 24 hour period either preceding (11 of 18) or directly following (7 of 18) a mood shift upward (defined as a change upward of 2 or more increments on our mood scale) (chi-square = 9.3, df=2; $p < .01$). Of the 7 that followed a change, several heralded yet another incremental increase in mood. Only 3 dreams of death were reported by unipolars, 2 of which accompanied a **downward** mood shift.

The dream anxiety levels, as measured by the Gottschalk and Glesser Anxiety Scale (Glesser, Gottschalk & Springer, 1961) tended to be somewhat greater in the bipolar group: bipolars' mean anxiety level per dream, 4.7; unipolars' mean anxiety level per dream 3.1.

4.6 DISCUSSION

The following methodological points merit a brief discussion. One problem with studying dream content in currently ill psychiatric patients is that self reports may be contaminated by dominant disordered affect. This is why we did not simply focus on the quality of the dreams (intensity, vividness, level of activity) but in our classification scheme also encompassed specific content such as death.

The treatments used in the hospital were potentially confounding. For example, if lithium had been given exclusively to bipolars and various classes of antidepressants were favoured for unipolars, no conclusion could be drawn about differences between these diagnostic groups that might not be explained as a drug effect. In the event, almost all depressed patients in our wards (and virtually all of our participants) regardless of detailed diagnosis, currently receive a specific class of antidepressants, selective-serotonin-reuptake-inhibitors (SSRIs) which are thought to have minimal effects on REM sleep. However, some report that fluoxetine increases dream intensity and nightmares. Because of ethical considerations we made no attempt to influence choice of drug.

The introduction of light therapy for improvement of mood was effective; however, whether we can safely say that it did not distort our REM sleep findings is arguable. We found no evidence that it did, but this was perhaps because its overall effects were diffused by inclusion of a group

getting low-light and no-light. In support of our hopeful assumptions, Partonen and colleagues (1993) reported that though light improved subjective reports of mood and sleep in SAD patients, they found no objective change in somnographic measures. Carrier and Dumont (1995) randomly assigned normal subjects to bright light exposure in the morning, afternoon and evening and monitored their sleep. They found changes in what they describe as subjects' propensity for sleep but report no detectible changes in SWS or REM sleep following light treatments. Also, in a separate analysis of the effects of light therapy on sleep (reported in Chapter 6), no significant changes were found from pre to post measures within-subjects following administration of light (Beauchemin, submitted for publication).

Finally, the nightcap, while an ideal device for this study, is not without limitations. It does not have an actual EEG measure so that the sleep record is totally reliant on peripheral measures (eye & body movements). Because of this, it cannot differentiate between stages 1 to 4 of NREM sleep. Also, the developers remark that in episodes of REM lasting <3 minutes, the device may conceivably mis-score this as arousal. A full scale polysomnographic recording would be more reliable, accurate, and comprehensive; but we think that the economy, versatility, availability, and unintrusive nature of the Nightcap were essential, and therefore outweighed its shortcomings.

Our hypotheses were for the most part supported, and have a claim to

further examination and testing. For those fascinated by dreams, the notion that they may have an important role in mood regulation is attractive.

Replication of aspects of our pilot study permit us to conclude that dreams of death are intimately associated with bipolar disorder. There is still debate about the nosological separateness of unipolar and bipolar illnesses; the finding that unipolar and bipolar patients are qualitatively different in terms of both REM sleep and dream content makes a further contribution to this debate. These markers (death dreams and state dependant REM latency) may prove to be useful diagnostic guides in distinguishing between the two depressive disorders. Death dreams occur in "normals" although quite rarely (Hall & Van de Castle, 1966); in the bereaved, commonly (Beauchemin, 1993); and apparently in some clinical categories facing possible demise (such as cardiac patients) (Smith, 1991). Only in bipolars have they been linked to an upward mood change.

The prolific reporting of death dreams in bipolar disorder cannot be entirely due to a preoccupation with death in depressed mood states, since these dreams are not common in unipolar depressives. An old psychoanalytic explanation of a mood shift toward hypomania was that the shift was an over reaction, the excessive result of a defence against depression, and striking examples of this are sometimes seen in practice. The dreams of death might trigger such a defence and lead to the upswing.

In line with Hartmann's views (1968b) the physiology of sleep

provides an ideal medium for a transition to mania. Specifically, increased catecholamine synthesis is afforded by REM sleep dreaming and in a predisposed individual this surge could cause a manic response.

The subject of death, awake or asleep, is undoubtedly a universally stressful theme. One possible sequence for the chain of events that may trigger a manic outcome might be as follows: a recent occurrence or event, sometimes even seemingly benign, may trigger a connection with a previously encoded affectively-charged experience from the past, perhaps a past loss. This topic is then synthesized into a dream experience. The dream experience then triggers an emotional and physiological reaction to its subject matter causing neurochemical and psychological changes which are carried over into the waking state. In a fragile or predisposed individual, this reaction might be tumultuous. Paradoxically, dreams of death might be viewed as positive, affording the medium for dreaming away depression.

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4.8 APPENDIX 1

REVISED DREAM CONTENT RATING SCALE

A. **MUNDANE , ROUTINE:** Contain little/ no affect, low activity & ordinary daily topics & people (eg: work, holidays) & does not contain qualities of B,C,D,E.

B. **UNSUCCESSFUL OCCURRENCES:** Dreamer experiences negative occurrence: loss sadness, misfortune, crying, unhappiness, rejection, failure, etc.

C. **BIZARRE:** contains unusual, improbable events eg: magic, delusions, aliens, flying, unusual creatures etc.

D. **VIOLENCE & INJURY**: physical / psychological threat, altercations, combat, mutilation bodily injury.

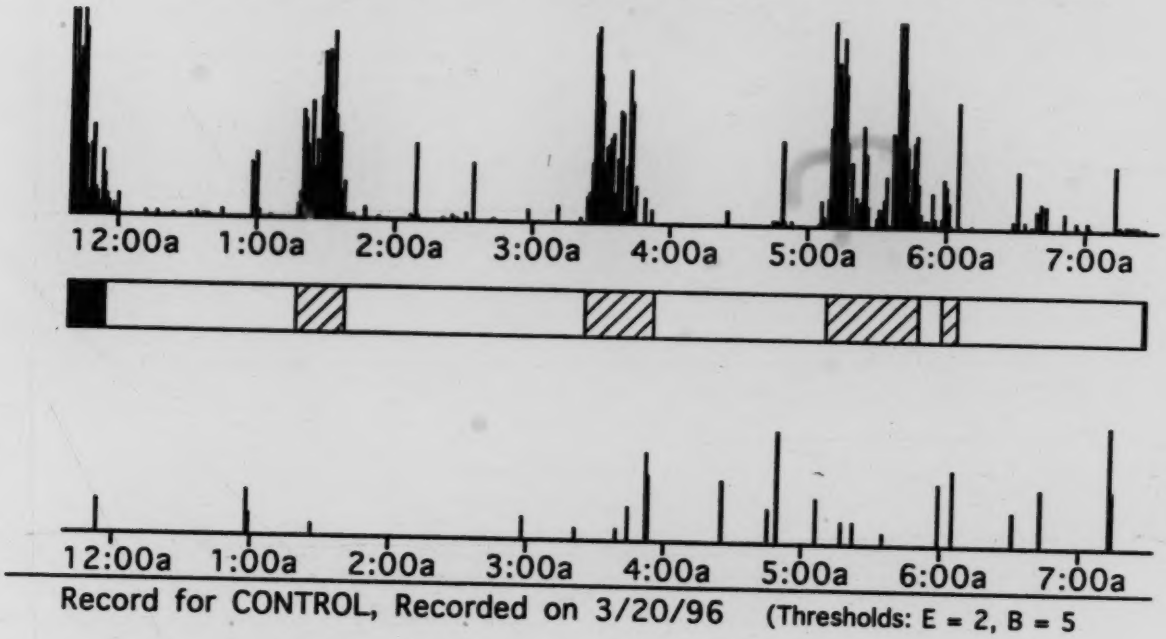
E. **DEATH**: Dream features death of self or other or threat of death to self or other. Also related elements of death (funerals, coffins, corpses, the deceased, etc.).

Bipolar patient's dream upon awakening manic:

I was at an old Victorian house with friends. It was rented for the day. Walked in through the bedroom ... had to feel your way into the bedroom. There was a door or staircase going up or down & you had to choose a bed. I chose top one on a slanted roof. I told my husband to take a picture of it. There were some guys coming down the road with a garbage can - singing Amazing Grace. They were digging a hole to bury a guy. My husband started digging a hole & said, "It's a sad day when you bury your father, isn't it." He was burying my dead father.
It's strange because I woke up feeling high!

SCORE: SUB-SCALE (E)
ANXIETY = 5

4.9 FIGURE 1
SAMPLE OF SLEEP RECORDING FROM NIGHTCAP (CONTROL)

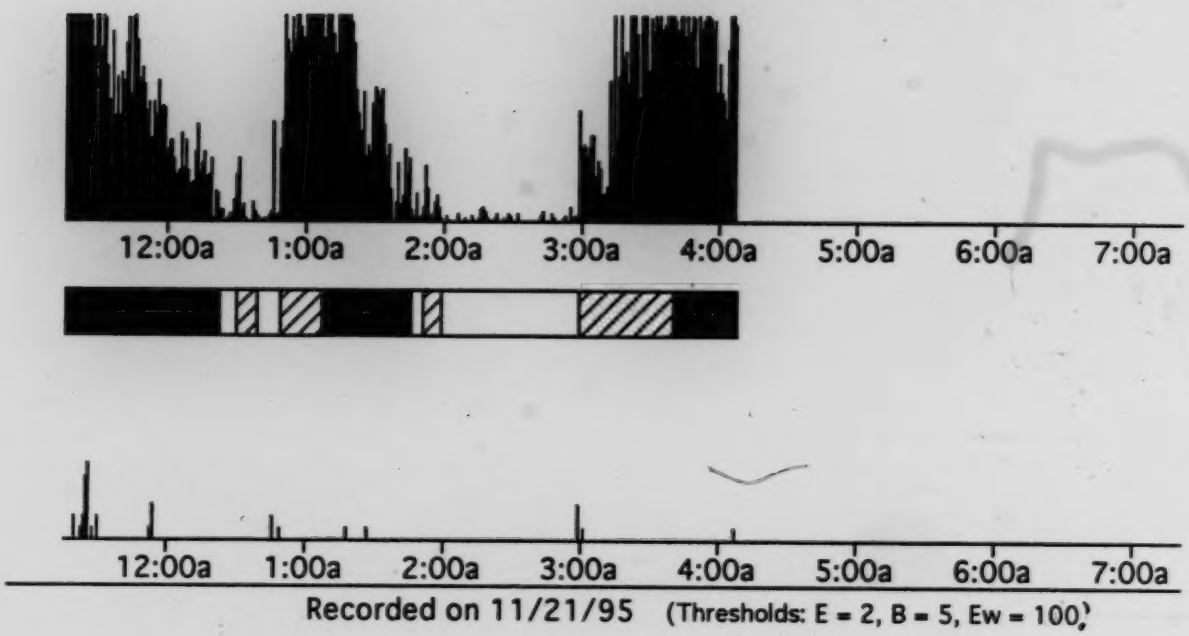


Record for CONTROL, Recorded on 3/20/96 (Thresholds: E = 2, B = 5

Total times
recorded: 468' sleep: 451' efficiency = 96.3%
Latencies
Sleep: 16' REM: 99'
Stage totals
Wake: 17' SWS: 348' REM: 95' BM: 8'
Sleep percents
SWS: 77.1% REM: 21.0% BM:= 1.7%
Total time percents
Wake: 3.6% SWS: 74.3% REM: 20.2% BM: 1.7%
Nocturnal awakenings: 0
REM periods (starting times)
99'(21') 225'(0') 330'(40') 380'(0')
Wake EM density: 71.6/min SWS: 1.3/min REM: 44.4/min
Wake BM density: 0.1/min SWS: 0.2/min REM: 0.4/min

SAMPLE RECORDING: NORMAL HEALTHY 37 YEAR OLD FEMALE

4.10 FIGURE 2
SLEEP RECORDING FROM NIGHTCAP: BIPOLAR PATIENT



Recorded on 11/21/95 (Thresholds: E = 2, B = 5, Ew = 100)

Total times
recorded: 292' sleep: 158' efficiency = 54.1%
Latencies
Sleep: 67' REM: 74'
Stage totals
Wake: 134' SWS: 82' REM: 76' BM: 0'
Sleep percents
SWS: 51.8% REM: 48.1% BM:= 0.0%
Total time percents
Wake: 45.8% SWS: 28.0% REM: 26.0% BM: 0.0%
Nocturnal awakenings: 1
REM periods (starting times)
74' (9') 93' (18') 155' (8') 223' (41')
Wake EM density: 105.7/min SWS: 2.2/min REM: 95.0/min
Wake BM density: 0.2/min SWS: 0.0/min REM: 0.0/min

BIPOLAR PATIENT: FEMALE AGE 49, AWAKENS MANIC
REPORTS NIGHTMARE OF DEATH

CHAPTER 5

5.0 STUDY 3: PHOTOTHERAPY IS A USEFUL ADJUNCT IN THE TREATMENT OF DEPRESSED INPATIENTS [1]

5.1 AUTHOR'S NOTE:

This study ventures away somewhat from the topic of sleep and dreaming but, nevertheless, reveals important findings engendered by the previous study. The reader will recall that in the previous study, light-therapy (phototherapy) was used in an attempt to promote upward mood swings in depressive participants. In order to make the most of this, a light efficacy trial was conducted simultaneously (using some of, but not all patients from Study 2).

5.2 INTRODUCTION

As noted earlier, Seasonal Affective Disorder (SAD) consists of a mild to moderate winter depression with a set of symptoms such as hypersomnia, carbohydrate cravings, weight gain, irritability and a period of elevated mood in the spring which sets it apart from most major depressions (Rosenthal, Sack, Gillin, et al., 1984). Its discovery led to a reconsideration of the therapeutic value of light, previously hallowed more in metaphors than in reports of experiments. Bright light treatment is now used routinely for the

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[1] A version of this chapter is published as: Beauchemin, K.M. & Hays, P. (1997). Phototherapy is a useful adjunct in the treatment of depressed in-patients. Acta Psychiatrica Scandinavia, 94,.

treatment of SAD.

The mechanism of action of light in this context remains largely unknown. There is evidence suggesting that light suppresses secretion of pineal melatonin (Lewy, Wehr, Goodwin, et al., 1986), which is directly implicated in modulation of circadian rhythms and hence of sleep. Circadian desynchronization may underlie the pathogenesis of mood disorders. There is no clear evidence for melatonin secretion abnormalities in SAD (Lam, Kripke, & Gillin, 1989) but apparently melatonin administration exacerbates symptoms in depressives (Carman, Post, Buswell, & Goodwin, 1976). Furthermore, the effect of bright light on sleep may be only subjective. Partonen et al., (1993) conducted a 5-day trial of bright light with a group of SAD patients, all of whom reported decreases in both depression and sleepiness, although these improvements were not associated with any objective changes in polygraphic sleep variables. Rao and associates (1990) demonstrated a pronounced increase of blood levels of serotonin following exposure to bright light. As is well known, serotonin is thought to be linked to depression, and this finding suggests an alternative mechanism (beyond the suppression of melatonin) for the effect of light on mood.

As mentioned previously, not only is the mechanism of action uncertain, but also the precise indications for the use of bright light therapy. Indeed, a recent controlled trial has cast doubt on its reliable efficacy in SAD (Levitt, Wesson, Joffe, et al., 1996). Some reports (Peter, Rabiger, Kowilak,

1986; Kripke, Gillin, Mullaney, et al., 1987; Kripke, Mullaney, Klauber, et al., 1992) indicate that light ameliorates non-seasonal depression, including bipolar depression (Papatheodorou & Kutcher, 1995). However, hypotheses about effectiveness are hard to test in controlled experiments because of the problem of keeping subjects blind to conditions, the placebo effects of even low intensity light, and either the ethical problems associated with deferring pharmacotherapy or the confounding effect of other continuing treatments.

Depression is a common disorder, and in some cases can be refractory or fatal. Any treatment which may be beneficial, especially one with negligible side effects, is worth assessing for efficacy, as it could be used in refractory cases as an occasional adjunct or, if generally helpful, routinely to expedite recovery.

With this in mind, we planned to test the effects of light-therapy as an ajuvant. We accepted that we could not do a standard controlled trial with a placebo group because a true placebo group would not be blind to its status. Instead, we used two groups, one of which received bright light and the other, light of lesser intensity. The reasoning was that since both types of light appear bright to the recipient, then greater and lesser degrees of dose related improvement in the two groups would provide oblique but compelling evidence of efficacy. In order to increase the likelihood of a differential response, we planned to use intensities above those which have generally been reported. There was no possibility for providing light-therapy alone

because the patients were sick and needed effective treatment, so we used the lights as adjuncts, leaving the other therapies undisturbed and determined by the patients' consultant psychiatrists without reference to us.

5.3 METHOD

5.3.1 Subjects:

Psychiatric admissions were monitored daily for eligible patients admitted over the course of the experiment, between September 1995 and February 1996, and those who qualified for inclusion were asked to participate. The inclusion criteria were a DSM-IV principal diagnosis of either Major Depressive Disorder, single episode, 296.2; Major Depressive Disorder, recurrent, 296.3; or Bipolar Disorder, depressed, 296.5 (American Psychiatric Association, 1994), none of which included a specific sub-type or chart reference to seasonality. The exclusion criteria were as follows: the patient's psychiatrist not wishing them to take part; impending electroconvulsive therapy; or release from hospital known to be imminent. At the time of recruitment, subjects were asked whether they wished to participate, and provided their written consent in accordance with our ethical approval protocol. A total of 22 subjects were recruited, of whom 19 subjects completed the trial. Of these, 10 fulfilled the criteria for bipolar disorder - depressed. The other 9 were diagnosed as having unipolar depressions (MDD). All of the subjects were recruited during the first week of their hospitalization, in most cases on the second day of hospitalization.

Subjects continued their medications throughout the trial of adjunct phototherapy. The drugs used are listed in Table 1.

5.3.2 Procedures:

Within each main diagnostic category, unipolar and bipolar, subjects were randomly assigned to receive high (10,000 lux) or low (2,500 lux) levels of light. Patients whose chart number was even were assigned to bright light conditions; and those with charts of odd numbers were assigned to low-light conditoned. Patients and hospital staff were blind to this designation, but not the researcher who was administering the light therapy (KB), i.e., the trial was single blind. The same type of full-spectrum (except ultraviolet) light box (SUN-RAY-II) was used in all cases, and the patients had no experience of light therapy. Differences in intensity were measured with a light lux meter, but because even 2,500 lux appears bright to the eye, all of the patients and their nurses thought that they were receiving full treatment. Participants were not given the opportunity to compare the two levels of light.

Over a 6-month period, the same researcher, (K.B.) attended each participant every morning except Sundays, between 0730 and 0930 over the 7 days of the treatment. Each received 30 minutes of light therapy daily at the predetermined level.

Mood was monitored during the light therapy. The same researcher, (K.B.) made a clinical assessment each day, and the patient used the corresponding subjective rating scale which we had devised for an earlier study (Beauchemin & Hays, 1995). As had been the case when we used this

method previously, patients' scores and those of the researcher were highly consistent (Spearman correlation, r=0.82). Mood was also assessed on Day 1 (pre-treatment) and Day 7 (post-treatment) using the Profile of Mood States - Bipolar Form (POMS-B). This test employs various bipolar subscale measures of mood, such as anxious/composed, depressed/elated, and tired/energetic (McNair, Lorr, & Droppleman, 1988). One minor change was made. Instead of referring to "the past week, including today", the instructions specified "today" only.

5.4 RESULTS

The raw scores on all six POMS subscales were combined to give a baseline global score of mood for each participant, and a post treatment global score, the differences between the scores representing changes in mood. The mean improvement in experimental subjects was +54.7 (SD=31.4), compared to +20.1 (SD=11.3) in controls (see 5.7 Figure 1). A two-factor analysis of variance was performed in order to determine whether the difference in mood change between the groups was significant, and whether there was an interaction effect with diagnosis. Diagnostic category (unipolar or bipolar) had no bearing on improvement in mood, the two groups responding equally well. Only assignment to bright light or low light was a key factor in the difference between the groups ($F=7.82$, $df=1,18$; $p<0.02$)

The averaged daily mood scores recorded by the researcher (K.B.) and patients showed that both groups started to improve from the outset, but did so at different rates.

5.5 DISCUSSION

The results reported here must be set alongside those methodological departures which distinguish the present study from a typical controlled double blind trial of a new treatment. We did not have a placebo-treated control group, because even relatively low levels of light have been reported to induce improvement, and even had that not been the case, the level of light which we used for the low-light cases was the same as that often employed for trials of light therapy. At the same time, if we had used truly ineffective levels of light, then the controls (as a result of discussing their experiences with fellow in-patients) might have realized they were receiving a low dose, and would have ceased to be blind participants. Our patients were blinded but the researcher (K.B.) was not. Because of this methodological shortcoming, the researcher refrained from spontaneously commenting on the patients' changing affect and, if they spoke of alteration, gave a neutral rejoinder. Furthermore, the pre and post outcome measures were completed solely by the patients, did not rely on clinical observations, and were scored only after the trial had been completed.

We propose that the only difference between the treatments for the two groups was that one received more light, and we consider that the differences in final mood can be ascribed to group assignment. In each instance (low and high dosages of light) a placebo effect will have been concealed in the

improvement scores. If this were the first trial of light therapy for depression, we would not be able to conclude that both levels of light were effective, since all of the improvement recorded for the low light group might have been due to a placebo effect. On the basis of previous trials of light therapy given at levels similar to those received by our low- light group, we feel that it is reasonable to assume that not all of the improvement recorded for our low-light group was due to a placebo response. It follows that improvement can be ascribed to light therapy of this kind, and that the improvement is dose-related. However, in future trials we will take the precaution of using three levels of light intensity, in order to minimize the hazards that follow from making assumptions.

Three patients dropped out of the experiment, in all cases because their mood had improved markedly. One had become hypomanic and all three were receiving high levels of light.

Some reports have stated that light-induced improvement is first detected at the third or fourth day of treatment (Lam, Kripke, & Gillin, 1989). The timing of the mood change is of theoretical interest. The informal daily assessments of mood change failed to demonstrate any latency in the subjects of the present study, as mood appeared to improve more or less steadily from the first day.

Our high-dose light therapy used more intense light than that which, from the literature, seems to be conventionally employed, but it is a

commonplace that doses of new remedies are often found to be too low as experience accrues. Our patients were depressed but did not have seasonal affective disorder, so that we may conclude that light therapy should be considered for the treatment of non-seasonal depressions as well as SAD. The bipolar and unipolar patients improved to a similar extent so that, correspondingly, it seems that light therapy should be considered for all serious depressions. As is the case with any effective antidepressant, some precautions would be indicated when such treatment is used on potentially hypomanic depressed patients. One patient had to discontinue participation in the trial at the request of her physician when she became hypomanic after 2 days of light treatment.

No conclusion can be offered about the efficacy of light therapy as a sole treatment for serious depressions on the basis of our data, and we do not consider that we could devise an experiment which could at once answer this question and meet our ethical standards. Because light therapy is apparently innocuous, it may be used in most cases where the patient is receiving conventional antidepressant therapy. We did not use light therapy on patients scheduled for ECT and two of the original candidates were dropped from the study when ECT was instituted. However, we see no reason why it should not be used in such circumstances, and a trial which used the number of ECT required at different levels of light therapy as one of the outcome measures would have the potential to provide unusually

compelling evidence.

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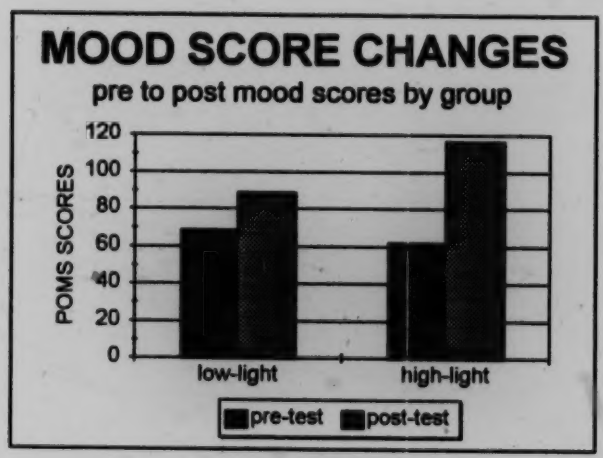
5.7 FIGURE 1:

AVERAGED GROUP SCORES ON PROFILE OF MOOD STATES BEFORE AND AFTER LIGHT THERAPY.



Profile of Mood States- Bipolar Form (POMS-B) is a self reported standardized mood inventory that measures six bipolar subjective mood states by sub-scale. POMS scores reported here were calculated by adding up raw sub-scale scores.

5.8 TABLE 1: PATIENT PROFILES

Ss N	Diag	Sex	Age	Light level	Drugs taken concurrent to light	Mood change
1	BP	F	36	Low	lithium, valproate, lorazepam	+16
2	BP	F	39	Low	fluoxetine, desipramine,lorazepam	+29
3	BP	F	49	Low	sertraline,clonazepam,lorazepam	+8
4	U	F	33	Low	haloperidol, benztropine, paroxetine	+1
5	U	M	43	Low	fluoxetine, flurazepam	+30
6	U	M	59	Low	temazepam, lorazepam, nitroglycerin	+30
7	BP	M	42	Low	lithium	+18
8	U	M	45	Low	fluoxetine	+29
9	BP	M	64	High	amitriptyline, lorazepam	+97
10	U	M	31	High	fluoxetine, lorazepam	+116
11	U	F	33	High	venlafaxine, fluoxetine, zopiclone	+69
12	U	F	33	High	fluoxetine, diazepam, pimozide	+28
13	U	F	21	High	sertraline	+32
14	BP	F	29	High	fluvoxetine	+37
15	U	M	46	High	sertraline	+28
16	BP	F	22	High	lithium, clonazepam, haloperidol	+64
17	BP	F	36	High	lithium, paroxetine, lorazepam	+19
18	BP	F	29	High	fluoxetine, lorazepam	+72
19	U	M	57	High	no drugs	+40

GROUP SUMMARY

Light level	N	diagnosis	Sex	x age	Mood change	SD
Low	8	BP=4, U=4	M=4, F=4	43	+20.1	11.3
High	11	BP=5, U=6	M=4, F=7	36	+54.7	31.4

BP=bipolar U=unipolar; Mood change: absolute increase in total POMS raw scores

CHAPTER 6

6.0 STUDY 4: LIGHT IMPROVES MOOD AND TIREDNESS RATINGS BUT NOT OBJECTIVE SLEEP MEASURES IN DEPRESSED INPATIENTS

6.1 INTRODUCTION

Phototherapy is an established treatment for SAD (Rosenthal, Sack, & Gillin, 1986), jet lag, and circadian phase sleep disorders (Terman, 1994); as I have demonstrated in the previous chapter and as have others previously, it is also an effective ajuvant for ameliorating depression in non-seasonals (Kripke, Mullaney, Klauber, et al., 1992; Lam, Kripke, & Gillin, 1989). Yet despite having established its efficacy, light's mechanism of action remains unclear. One hypothesis attributes light-therapy's ameliorative capacities to its regulation of circadian rhythmicity (Wetterberg, Beck-Friis, & Kjellman, 1990). This hypothesis is based on the belief that a circadian phase advance may underlie the pathogenesis of depression and account for the pervasive REM sleep abnormalities found in depressives (Lewy, 1987). However, light-therapy in the morning, the time most commonly reported as effective, is said to phase advance circadian rhythm (presumably in the direction of the existing pathology in most MDD cases).

Light suppresses melatonin (Lewy, Wehr, Goodwin, et al, 1980) which is directly implicated in circadian regulation. However, there is no clear evidence for melatonin secretion abnormalities in SAD (Wetterberg et al.,

1990). In non-seasonal depressions, Beck-Friis and colleagues present evidence for a low melatonin syndrome in depression (Beck-Friis, Kjellman, Aperia, et al., 1985). However, this may be a reflection of another primary neurochemical imbalances as functional deficiencies of noradrenaline, serotonin, or both, have the potential to lower pineal melatonin production (Arendt, 1989). Lewy et al., (Lewy, Wehr, Gold, et al., 1978) have reported a state-dependant relationship between melatonin and mood in bipolars, with higher levels of melatonin in mania and lower levels in depression. Yet, melatonin administration, at least in large amounts, apparently exacerbates symptoms in depressives (Carman, Post, Buswell, & Goodwin, 1976), apparently in contrast to beneficial effects hailed in normals (Reiter & Robinson, 1995).

As discussed previously at length in the review chapter, sleep is drastically altered in pathologies of mood and melatonin is said to regulate circadian rhythm and function as an effective soporific agent. Hence, given that light inhibits melatonin secretion and improves mood, one would anticipate that mood improvements would be directly related to measurable changes in sleep. However, the effect of bright light on sleep in mood disordered subjects may be of a subjective nature, as improvements in mood and sleep ratings in SAD patients were not associated with any objective changes in polygraphic sleep variables (Partonen et al., 1993).

Rao and associates (1990) have demonstrated a pronounced effect on

blood levels of serotonin following exposure to bright light, hence, this may be an alternative mechanism that may account for positive effects of light on mood. However, Partonen (1994) hypothesizes that the antidepressant effect of light are due to a normalization of corticotropin-releasing factor (CRF) which is altered in SAD patients.

A study to test the dose dependant effects of light therapy on mood was already in progress (see chapter 3), and as such, facilitated this additional measure of sleep before and after light administration. In accordance with ethical guidelines, no prospect of doing light therapy alone existed, since the patients were severely depressed. The lights were used as adjuncts, with other therapies undisturbed and decided by the patients' psychiatrists. This was not considered an insurmountable confound as sleep measures were compared using a within subjects design.

Sleep was monitored the night before commencement of light therapy and again upon completion. This was done using the NIGHTCAP. The Nightcap, which is reviewed in previous chapters, is a reliable and compact computerized ambulatory device that records eyelid and head movements and based on an algorithmic ratio of these two parameters can determine sleep latency and REM and non-REM sleep stages (Mamelak & Hobson, 1989).

6.2 METHOD

6.2.1 Subjects:

All patients were hospitalized for a depressive episode and had voluntarily consented to participate in the light-study. A sub-set of these patients consented to this additional study, i.e., to have their sleep recorded. Inclusion criteria were a DSM-IV principal diagnosis of either Major Depressive Disorder (MDD), single or recurrent episode or Bipolar Disorder, depressed (American Psychiatric Association., 1994). None of these patients had a history of seasonality. All subjects were recruited within the first week of their hospitalization, in most cases, on the second day of hospitalization. Nineteen subjects completed the light trial. An attempt was made to monitor sleep in all patients recruited, but many did not comply for various reasons. In some cases, the monitoring was omitted because of severe suicide risks and in others because of patient refusal. Several nights were lost to equipment failure. This resulted in only 10 subjects (6 bipolar patients and 4 unipolars patients) having complete data for pre and post sleep recordings.

Subjects continued their medications throughout the trial of adjunct phototherapy. All were taking selective serotonin reuptake inhibitors (SSRIs) with the exception of 3 on lithium. In all cases, these drugs were started a considerable amount of time before the light-therapy was instituted so that any direct effects of the drugs on sleep should have already occurred.

6.2.2 Procedures:

Each participant was attended every morning except Sundays for about thirty minutes, between 0730 and 0930 for 7 days of treatment. Each patients received 30 minutes of light therapy daily (at intensities of 2,500 or 10,000 lux). Sleep was recorded on the night preceding commencement of light therapy and again on the night of the last treatment day.

Mood was assessed on Day 1 (pretreatment) and Day 7 (post-treatment) using the Profile of Mood States - Bipolar Form (POMS-B). This test employs various polar subscale measures of mood such as anxious-composed, depressed-elated, and tired-energetic (McNair et al., 1988). Subjects were asked to complete this test according to their prevailing mood on that particular day.

A multiple T-test (using SPSS) was used to determine pre to post changes within-subjects on measures of: total mood ratings, tired versus energetic ratings, REM percent, REM latency, total sleep time, and sleep efficiency.

6.3 RESULTS

Total mood scores improved significantly from pre and post measures (T=4.2, df, 9; p<.002). Analysis of the specific sub-scale "tired versus energetic" alone also showed significant improvements (T=4.3, df, 9; p<.002).

Four measures of sleep were compared within subjects from pre and post measures: total sleep time, sleep efficiency, REM-latency and REM percent. No significant differences were found in any of these measures, although REM-latency showed a tendency to decrease with mood improvements in the unipolars and increase in the bipolars (a finding that was significant in a larger patient sample reported elsewhere (Beauchemin & Hays, 1997). Similarly, total sleep time tended to decrease with mood improvements in bipolars and increase in unipolars.

6.4 DISCUSSION

It would appear on the basis of these preliminary findings that light-therapy improves patients' rating of mood and of tiredness; however, these improvement do not appear to be the direct result of a corresponding improvement in sleep as might be expected.

These findings are somewhat unexpected in light of the usual proposed circadian mechanism of action for light-therapy. It may well be that the regulation of melatonin ameliorates symptomatology in depressives. Light suppresses melatonin (Lewy, Wehr, Goodwin, et al., 1980) and an increased sensitivity to light suppression has been documented in bipolar patients (Nurnberger, Berettini, Tamarkin, et al., 1988). This suggests that bipolars react swiftly to the induction of light by suppressing melatonin. Theoretically, this could lead to increased awakenings which is a known precipitant of mania. Alternately, initial daytime melatonin suppression could lead to an increased nighttime peak. However, if this were the case, it should be evidenced in an improvement in sleep continuity. It is unclear at this point what the physiological consequences are, but it would be logical on the basis of what is known to assume that some alteration in sleep should accompany light-therapy. However, at least at this preliminary stage, improvements in sleep appear to be subjective or secondary to mood improvements as no objective sleep changes were detected following administration of light-therapy. If changes in sleep do occur from light,

perhaps it alters some unmeasured parameter such as delta sleep which could not be measured with the Nightcap. Conversely, perhaps the effects of light on sleep are weak and, as such, require a larger sample size for statistical detection. But given that no changes were reported by Partonen's SAD group (1993), or in normal subjects (Carrier & Dumont, 1995) even with full polysomnography, perhaps the decrease in tiredness reported by depressives following light administration is a by-product of an overall improvement in mood and not the direct result of improvements in objective sleep measures. More research in this area could hardly fail to produce interesting results.

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CHAPTER 7

7.0 STUDY 5: SUNNY HOSPITAL ROOMS EXPEDITE RECOVERY FROM SEVERE AND REFRACTORY DEPRESSIONS [1]

7.1 AUTHOR'S NOTE

The following study constitutes an additional inquiry into the effects of light therapy. It was not planned as part of the series undertaken for this thesis, as such, but was engendered from observations made while conducting the previous studies.

7.2 INTRODUCTION

Apart from its use in SAD, light therapy is also said to help other types of depression (Kripke, Mullaney, Klauber, et al., 1992). Bright light is presumed to exert its effects neurohormonally, by suppressing melatonin which is involved in the entrainment of circadian rhythm (Wetterberg, Beck-Friis, & Kjellman, 1990) and hence, the sleep-wake cycle. However, the precise mode of action is unknown. Patients who are admitted to our hospital with depression have either severe, often suicidal, depressions or depressions which are refractory to conventional remedies. They receive a variety of medications and other treatments.

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[1] A modified version of this chapter is published as: Beauchemin, K.M., & Hays, P. (1996). Sunny hospital rooms expedite recovery form severe and refractory depression. Journal of Affective Disorders, 40, 49-51.

In Alberta the sun shines year round for a total of 2,300 hours, the winter sunlight being intensified over a four month period by reflection from the snow. Our hospital is constructed so that each inpatient room has a large window with a view. Some rooms overlook an airy glass-roofed courtyard, and others have an outdoor view. Our psychiatric unit is on the fourth floor, and of those rooms with an outdoor view, all face due east and get full unimpeded sunlight: these are the brighter rooms. Turning to the remaining rooms, one faces north; the rest either face the indoor courtyard or face west and receive no direct sunshine because a large structure intervenes: these are the dull rooms. By chance, then, the orientation of the inpatient units is such that the level of illumination in all rooms is either bright and sunny, or sunless and relatively dim.

Our two psychiatric wards 4F3 and 4G2 are symmetrical about their north to south long axes, with the nursing stations in the geometrical centres, and the two rows of rooms on each ward are almost identical to each other. None of the admitting doctors has patients mainly in one or other side of the ward, and new patients are allocated in a non-systematic manner, according to which bed is empty. The ease with which patients can be observed in a room depends on the closeness of the room to the nursing station, but not on which side they are placed. There is no grouping or clustering of patients according to diagnosis. We note, however, that the vacating of hospital beds may not be a random process.

Patients admitted to the unit are of course given a final diagnosis at the time of discharge, and their admission and discharge dates are recorded. These circumstances together made up a natural experiment, enabling us to test the hypothesis that depressed patients in sunny rooms would stay in hospital for a shorter term than those in rooms without direct sunshine.

7.3 METHODS

We abstracted data for all admissions over a two year period (Oct, 93 to Sept, 95) with a principle International Classification of Disease (US Department of Health and Human Services. 1980) diagnosis of depression (296.2, 296.3, 295.5, 311), with the exception of patients with anorexia nervosa, whose length of stay is determined by factors other than mood, and patients whose length of stay was under six days. We assumed that those who were discharged after less than six days were admitted overcautiously or had improved spontaneously. We designated the illumination in each room as bright or dim. Some patients had been moved from bright to dim rooms or vice versa during the course of their stay, and these were also removed from the analysis. Where a patient had been admitted more than once over the two year period, we considered only the last admission.

7.4 RESULTS

Reviewing the remaining 174 admissions, there was a total group average of 18.1 days length of stay, with a standard deviation of 11.88, and a range of 6 to 86 days. Patients in brightly lit rooms stayed an average of 16.9 days, whereas those in dimly lit rooms stayed 19.5 days, with a mean difference of 2.6 days. This difference was consistent over the seasons. A Z-test comparing sample means showed the difference to be significant ($Z=1.4$; 1 tail, $p<.05$). We returned to the wards to try to discover a reason other than relative brightness which could account for the differences in length of stay. We failed to do so.

7.5 DISCUSSION

Depression is the most common symptom, diagnosis and cause of admission in psychiatric practise, and is the commonest antecedent of suicide. This study is of theoretical interest, and has obvious implications for reduction in suffering, the confounding of inpatient drug trials, the optimal siting and orientation of dwellings, new hospital design, and the utilization of existing units. If the findings of this natural experiment are valid, the resulting savings would make a palpable reduction in health care costs.

7.6 REFERENCES

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CHAPTER 8

GENERAL DISCUSSION

8.1 SUMMARY OF RESULTS

On the basis of the original research reported here, it may be concluded that:

(1) prevailing mood state is reflected in dream content;

(2) dreams of death mark the transition from depression to mania in bipolar disorder;

(3) sleep is pathologically altered in affective disorders;

(4) REM latency is shortened in both unipolar and bipolar depression but tends to increase as mood improves in bipolar disorder and remains stable or even decreases with mood improvements in unipolar depressives.

(5) Exposure to bright light, whether artificial or natural, is an effective adjuvant antidepressant for both unipolar and bipolar depressives. The mechanism by which it does so remains unclear but preliminary findings suggest that it does not alter sleep directly although a subjective improvement in sleep is reported. Light exposure can also precipitate hypomania or mania in bipolars.

8.2 CONCLUSION

8.2.1 Physiological considerations:

These findings, taken separately, are in and of themselves straightforward; however, how they might be explained in some interconnected fashion remains both elusive and speculative. First, we might ask: what do all known precipitants of mania share? Presumably, if a sole neurochemical underpinning of mania exists, then all these factors must share a common final pathway. Some of the apparent precipitants of mania either demonstrated in this thesis or reported by others are: (1) dreams of death; (2) light-therapy; and (3) prolonged sleep deprivation. There is also some evidence that childbirth can precipitate both mania and depression. Although some other factors such as amphetamines and cortisol have been implicated in mania, the discussion will be limited primarily to the aforementioned factors which are more directly related to the studies reported in this thesis.

At first glance, dreams of death as a manic-promoting factor appear incompatible with the sleep deprivation hypothesis; presumably one must sleep in order to dream. Moreover, light-therapy appears, at least superficially, to hold little in common with sleep-deprivation and dreaming.

Delving further, we might ask: what neurochemical changes might underlie all these phenomena? As was reviewed in previous sections, dreams, particularly those with a high level of anxiety, can trigger a

sympathetic (adrenergic) discharge. Sleep deprivation has been shown to increase synaptic sensitivity and to increase catecholamine (specifically dopamine) and opioid levels in animals (Fadda et al., 1993).

REM sleep deprivation has been associated with improvement of mood states in depressed subjects (Vogel et al., 1977). When a group of depressed bipolar patients were sleep deprived for one night, most had switched into hypomania or mania by the following day (Wehr, Sack & Rosenthal, 1987).

Recently, Fadda et al., (1993) demonstrated that sleep deprivation in rats leads to a hyperactivation of the endogenous opioid system, suggesting that the ameliorative effects of sleep deprivation on mood may be related to increased endogenous opioid activity.

Light-therapy has demonstrated effects on melatonin and possibly serotonin (Rao, Muller-Oerlinghausen, & Volz, 1990) but neither of these appears to account for mania. Light travels via an indirect sympathetic pathway from the eye to the pineal gland (see 8.4 Figure 1). There is evidence that this transmission is mediated by glutamate and noradrenaline. There is also some evidence suggesting an opioid connection in melatonin transmission; sigma-opioid receptors are found in high concentrations in the pineal gland, although the functional implications of these receptors remain undetermined (Reiter, 1991). The opioid receptor blocker naltrexone demonstrably antagonizes immunostimulatory effects of melatonin (Maestroni, Conti, & Pierpaoli, 1987). Therefore, one possible commonality

between light and sleep deprivation may be a mutual effect on the endogenous opioid systems. But does dreaming share this factor? It is of interest to note that in the early 19th century, Thomas DeQuincy wrote about the vivid dreaming experiences he had while taking opium.

Although there is only minimal evidence for the role of endorphins in REM sleep, nothing that we know contradicts this proposition. This small body of evidence is reviewed below. There is also evidence that stress causes both sympathetic arousal and release of endorphins. Dreaming, particularly of death, could be construed as stressful. It is likely that our psychological and physiological reactions to dream content are the same as if the situation in the dream was actually happening. That this can happen is demonstrated by the experience that nearly everyone has had of waking in the middle of the night from a nightmare to find his or her heart pounding, sweaty palms, shallow breathing, etc, that is, an intense sympathetic reaction.

8.2.2 A possible role for endogenous opioids and REM sleep

The endogenous opioid peptides can act as neurotransmitters, neuromodulators and neurohormones (Pert et al., 1981). β-endorphin has known modulating effects on both neurotransmitter and hormonal systems (van Praag & Verhoeven, 1981). The endogenous opioids have been shown to inhibit ACh, (the primary neurotransmitter involved in the initiation of REM sleep) and to increase the release of dopamine (Spanagel et al., 1991).

Morphine increases dopamine (DA) and 5-HT levels in rat brains (van Ree & Terenius, 1978). Opiate receptors and their endogenous ligands appear to be involved in the regulation and synthesis of brain monoamines (Ahtee et al., 1978). This suggests that endorphins might function as an intermediary step in "turning off" REM sleep, which subsequently causes an increase in monoaminergic and catacholinergic activity. Endorphins also show measurable respiratory, cardiovascular, and thermoregulatory functions (Pert et al., 1981), all of which undergo important changes in REM sleep.

Opioid pathways abound in the brain. β-endorphin is present in distinct fibres projecting through hypothalamic areas into the diencephalon and pons (van Ree & Terenius, 1978). The locus ceruleus (LC), is the postulated "REM off" control site in Hobson's RI model. This area is also dense in opioid receptors (Simon & Hiller, 1989). Electrophysiological studies show high opioid receptor binding in the LC, whose activity can be inhibited by morphine (Verebey & Gold, 1985). In addition to the LC, the raphé system is also assumed to play an important role in the regulation of REM sleep. Jones (1994) reports that enkephalin is co-localized with 5-HT in the raphé neurons. Furthermore, the specific postulated site of REM generation (mPRF) appears to have opioid receptors as well; morphine injection into the nucleus gigantocellularis of the PRF result in potent analgesic effects (Pert et al, 1981). β-endorphin containing neurons project laterally from the nucleus of the solitary tract to many pontine reticular sites

including the LC. In the medulla, they innervate the nuclei raphe magnus, reticularis gigantocellularis, paragigantocellularis and reticualaris lateralis (Simon & Hiller, 1989). It would appear that all the known sites reputed to be involved in the control of REM sleep are also associated with opioid activity. Moreover, several research teams have postulated endorphin activity as a potential trigger of mania (Janowsky, Judd, Huey, et al, 1983) and in response to fear (Hunt, Adamson, Egan, et al, 1988). In human females, endorphin levels increase throughout pregnancy and peak during labour. It has been speculated that the tenfold drop from peak endorphin levels immediately following childbirth may be an instigating factor in postpartum depression (Liska, 1990). If dreams of death are viewed as either fear or stress provoking and if the "off" mechanism for REM sleep is modulated by endorphins, then endorphin release may trigger mania, either directly or indirectly, such as via subsequent increases in dopamine levels. This model might account for the abrupt manifestation of mania upon awakening from a dream of death.

This hypothesis is, of course, only tentative at this point, but is offered as one possible connection between the entire findings of REM sleep, dreaming, light-therapy and sleep deprivation.

8.2.3 Psychological considerations:

One way of connecting all the factors dealt with to this point is set out in a diagram in section 8.5 (see Figure 2). In this model, all factors are illustrated with the connections between them drawn out. The postulated contributors to bipolar disorders are shown, starting with a genetic predisposition. This diathesis (genetic predisposition) might later be expressed by a trigger - such as the occurrence of prolonged or acute stress (such as an early loss). It is interesting to note that an early loss, particularly of one's mother, is a significant predictor of adult depression. Barrett (1979) writes that:

> loss of mother before age 11 plays two roles - as a vulnerability factor it increases risk of depression, and as a symptom-formation factor it influences the form and the sensitivity of depression according to whether the loss was by death or by separation (p.117).

As dreaming might be viewed as a form of regression to past memory, dreams of death may be the latent expression of this psychic trauma. Reexperiencing this type of stressor in a dream may cause a neurochemical reaction that, in a susceptible person, leads to psychosis. It is interesting to note, as mentioned previously, that Beck-Friis and colleagues (1985) reported a low melatonin syndrome in depression and one predictor of this syndrome was early parental loss.

The observation that dream content is directly reflective of material derived from emotionally important experience is supported by the dream studies reported here. This is not an original idea, but one attributable to Freud; however, the basis of Freudian dream theory was to suggest that only the latent content, expressed as wish-fulfilment, reflected psychic trauma or emotional turmoil. Dreams may directly reveal the dreamers emotional state; however, most modern theorists assert that it is seldom necessary to look for a hidden (or latent) meaning, at least in a "normal" dreamer. Yet the dreams of death, found so frequently in bipolar-disordered patients in relation to an upswing in mood, seem to suggest that the manifest or obvious content in this particular case is incongruous with underlying mood. A less surprising relationship might be to find dreams of death in association with depression and not the transition to mania; however, this was not the case.

In an older study reported by Hauri & Van de Castle (1970), level of physical activity in dream content did not reflect corresponding physiological arousal, whereas the emotionality within the dream was significantly related to physiological intensity. Moreover, adrenaline injections (compared to saline injections) prior to REM sleep yields significantly more bizarre, emotional and vivid dreams (Block Lewis, 1981), suggesting that autonomic arousal accompanies intense dreaming.

Hartmann (1996) theorizes that dreams are like explanatory metaphors that contextualize a dominant emotion. He writes that:

> This entire process is probably functional. The dream functions to spread out excitation or reduce 'computational energy' and does this by cross-connecting and 'weaving-in'. This has an immediate function in 'calming a storm' or reducing a disturbance, and a longer term function relating to memory ... (p 147).

Given the pronounced effect of dreaming on mood, (and of mood on dreaming) one might postulate that the elusive function of dreaming is to process ongoing emotional experience through memory consolidation with previous and similar schema and by doing so, ensuring the homeostasis of mood and psychological well-being.

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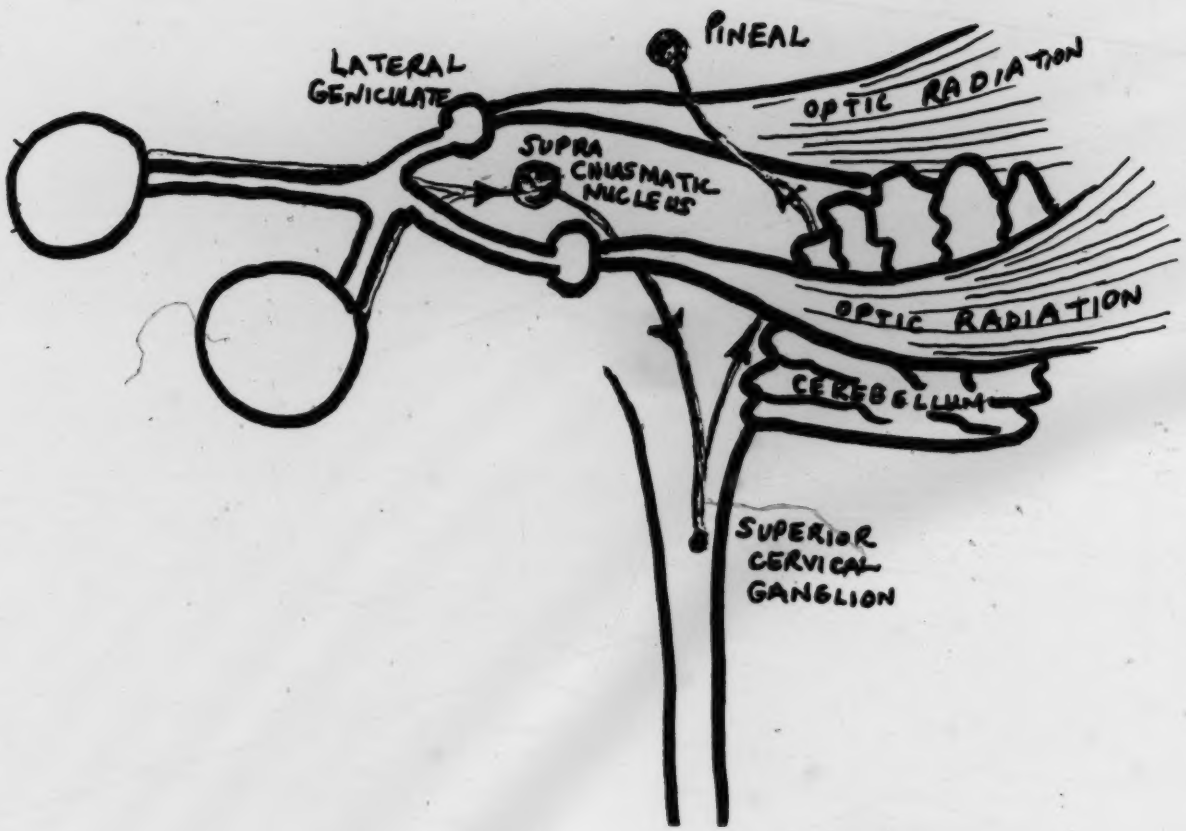
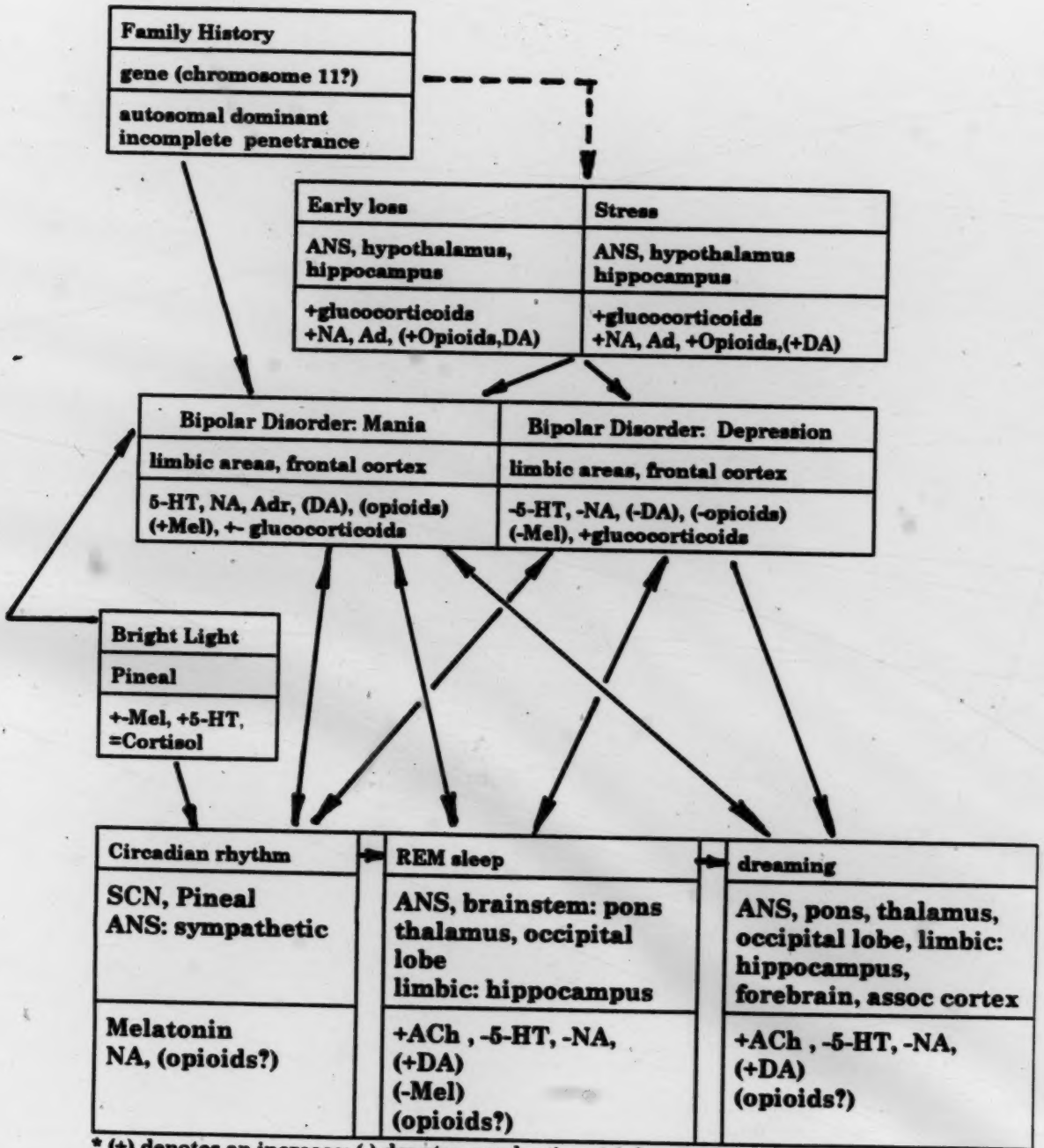
8.4 FIGURE 1

PATHWAY OF LIGHT TO PINEAL VIA SYMPATHETIC NERVOUS SYSTEM



8.5 FIGURE 2:
Theoretical Model of BD: Causes, Correlates, & Substrates



* (+) denotes an increase; (-) denotes a reduction; (=) denotes balancing.